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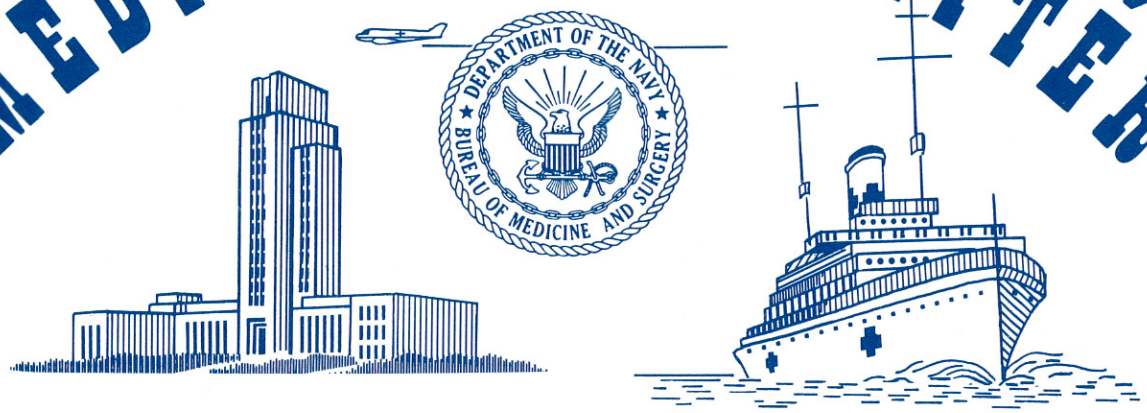
UNITED STATES NAVY MEDICAL NEWS LETTER



Vol. 53 June 1969 No. 6

CONTENTS

United States Navy
MEDICAL NEWS LETTER

Vol. 53 June 1969 No. 6

Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390 (Code 38), giving full name, rank, corps, old and new addresses, and zip code.

The issuance of this publication approved in accordance with NAVEXOS P–35.

AN OPEN LETTER FROM THE SURGEON GENERAL TO ALL HOSPITAL CORPSMEN ON THE 71ST ANNIVERSARY OF THE FOUNDING OF THE HOSPITAL CORPS

As Surgeon General of the United States Navy, I am pleased to extend my most sincere congratulations and very best wishes to the men and women of the Hospital Corps of the Navy on your 71st Anniversary.

Since the beginning of the Corps, 17 June 1898, corpsmen have served the Navy and Marine Corps afloat and in the field in a most outstanding manner.

From the beginning of the present conflict in Southeast Asia, your corps has expanded rapidly to a current strength of over 31,000. My personal apppreciation for the experience and guidance afforded the newer members of the corps by the senior petty officers cannot be overemphasized. The response by all members of the corps to the increased demands placed upon the Navy Medical Department has been a source of great pride to me. Your superb performance in Vietnam and throughout the world is a tribute to the Navy.

I am confident that you will continue to serve our nation in peace and war in the best traditions of the Naval Service as you have done so ably in the past. Congratulations and WELL DONE!

G. M. DAVIS
Vice Admiral, MC, USN
Surgeon General

MEDICAL ARTICLES

DRUG RESISTANCE OF BACTERIA*

Leon D. Sabath, MD. Brit Med J 280(2):91–94, Jan 9, 1969.

Drug resistance of bacteria is a major medical problem because it severely limits the usefulness of virtually all known antimicrobial agents and often necessitates the administration of highly toxic drugs when the more acceptable ones are found to be ineffective. Occasionally, cultures from patients with bacterial infections yield organisms resistant to all the drugs used in sensitivity tests. The following remarks pertain primarily to currently practical aspects of the general problem. Few clinically applicable suggestions have yet emerged from recent studies of the mechanisms of resistance and its genetic control; accordingly, these interesting subjects are only briefly summarized here.

Extent of the Problem

At Boston City Hospital multiple drug resistance is now common among strains of *Staphylococcus aureus* (Table 1) and in most species of gram-negative bacilli (Table 2) when tested by a single-disk method in conjunction with routine management of infections caused by these agents. Not shown are the results with *Pseudomonas aeruginosa,* which was rather consistently susceptible to polymyxin B and gentamicin; relatively few other agents could be expected to be effective 95 percent or more of the time against any of the organisms listed.

These patterns of drug resistance may show rather abrupt changes, particularly when new antibiotics are introduced or when there are changes in the customary usage of antimicrobial agents within a hospital or community. Understandably, considerable hospital-to-hospital variation in such patterns of resistance may exist, and it seems advisable for each institution to monitor its own drug-resistance problem so that such information may be used in the selection of antibiotics, particularly for fulminating infections.

TABLE 1.—*Frequency of Antibiotic Resistance in* Staphylococcus aureus *at the Boston City Hospital, 1966–1967 (482 Strains—Single-Disk Method)*

Antibiotic	Percentage of Strains Resistant
Penicillin	83.6
Tetracycline	38.2
Erythromycin	31.4
Kanamycin	20.3
Chloramphenicol	8.0
Lincomycin	6.6
Nafcillin	2.9
Cephalothin	0.4

Clinical Treatment Resistance

Treatment failure of bacterial infections is by no means limited to infections due to organisms resistant to the drugs being used. The cause of treatment failure when the organism is sensitive is usually either the way in which the drug is used or something peculiar to the patient (as indicated below). Because the results may be equally unsatisfactory in treatment failure of either kind, it is as important to recognize the causes listed in the next paragraph as it is to detect drug resistance.

Six causes of treatment resistance occurring when the organism is sensitive to the drug being used. In the first place, treatment begun too late (that is, after irreversible processes have been initiated) may yield poor results, even though the organism is exquisitely sensitive to the drug being used. Secondly, suboptimal use of effective antibiotics may simulate drug resistance (for example, dosage too small, administration too frequent, duration of therapy too short, route of administration inappropriate, and necessary adjuvant medications or procedures not used). Thirdly, organisms present in the host in an altered metabolic state (for example, dormancy) or as variant forms (for example, protoplasts, spheroplasts or L-forms) usually have different drug susceptibilities than their classical bacterial forms; the dormant cells resist drugs that require growth to act, whereas the variant forms mentioned (which require special mediums for isolation) are highly resistant to antibiotics that interfere with cell wall formation (the penicillins and cephalosporins, bacitracin and vancomycin) and are usually much more sensitive to most drugs acting by other mechanisms (such as erythromycin, tetracycline, and the aminoglycoside antibiotics.) Fourthly,

* From the Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School (address reprint requests to Dr. Sabath at the Harvard Medical Unit, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118).

Aided by grants (AI-00023 and TOI-AI-00068) from the National Institute of Allergy and Infectious Diseases (Dr. Sabath is the recipient of a United States Public Health Service Research Career Development Award from the National Institute of Allergy and Infectious Diseases).

TABLE 2.—*Frequency of Antibiotic Resistance in Some Gram-Negative Bacilli Isolated at Boston City Hospital in September and December, 1967 (284 Strains—Single-Disk Method)*

Organism	No. of Strains Tested	Percentage of Strains Tested Resistant to Antibiotic Indicated							
		Strepto-mycin	Tetra-cycline	Chloram-phenicol	Kana-mycin	Poly-myxin B	Genta-micin	Ampi-cillin *	Cepha-lothin *
Escherichia coli	108	50	61	15	11	1	2	57	60
Klebsiella sp.	95	73	62	55	33	1	4	81	35
Enterobacter sp.	19	58	58	47	26	5	0	95	95
Proteus sp.	32	44	91	28	16	63	0	33	20
Serratia sp.	30	70	97	60	47	83	0	86	86

* Not tested against 4 strains of serratia sp. & 16 strains of proteus sp.

some substances present in the patient either as medication administered or as the result of pathologic or physiologic processes may antagonize the action of some antibacterial drugs; thus, bacteriostatic drugs antagonize the killing action of penicillins and cephalosporins, pus and some metabolites antagonize sulfonamides, and the presence of an acidic or basic environment may change the effect of drugs that have strikingly different activities at different physiologic pH's (as indicated below). Fifthly, barriers preventing adequate contact between organisms and drug are at times responsible for poor results; examples are the "blood-brain" barrier in meningitis, intracellular or intraocular organisms when the drug used poorly enters those compartments, empyema and abscesses. Finally, naturally occurring (congenital or acquired) and man-made (drug or radiation induced) states of depressed host defense mechanisms (cellular or humoral) are conducive to treatment failure as well as to increased susceptibility to infection.

It is as common for the organisms to persist in gram stains and cultures taken during therapy when treatment failure is from the second cause (occasionally the third), and the fourth, fifth and sixth as it is when treatment failure is due to drug resistance. In many cases clinical improvement can be effected if likely causes of treatment failure are anticipated or recognized. In treatment failure due to drug resistance efficacious alternative drugs are not always available. Only a thorough knowledge of the patient, the pathologic process, the clinical pharmacology of the relevant drugs and the limitations of antibiotic-susceptibility testing in the laboratory will permit a distinction to be made between treatment failure due to drug resistance and that from other causes; the remedies are clearly different.

Detection of Drug Resistance and Drug-Susceptibility Tests

The conclusion that an organism is resistant to a given antibiotic is a somewhat arbitrary decision. In most hospital laboratories it is based on the result of a single-disk antibiotic-susceptibility test; this has proved to be a valuable tool for the detection of drug resistance and the guidance of therapy in spite of some serious shortcomings. Oddly enough, the laboratory decision that a strain is resistant to a given antibiotic is based on data from patients or subjects, in that the approximate range of antibiotic concentrations achievable with customary doses in human beings is taken as the dividing line between what is sensitive and what is resistant. Thus, although an organism may be readily inhibited in the laboratory by a low antibiotic concentration, it is considered to be resistant if those concentrations are not feasible in patients.

Two specific infections in which routine sensitivity testing may be misleading are bacterial endocarditis and urinary-tract infections. *Bacterial endocarditis* has only rarely been cured with bacteriostatic drugs; therefore, this infection caused by any bacteria may be assumed to be resistant to all the bacteriostatic drugs, irrespective of results of the disk-sensitivity testing for inhibition. *Urinary-tract* infections yield organisms that should be considered separately because some antibiotics that appear in the urine at concentrations many times higher than those found in the blood—for example, the penicillins—may be useful in treating urinary-tract infections even though the laboratory test (if performed with disks that relate to serum levels) indicates that the organism is "resistant." A second reason for special consideration is that urine is often at pH 5 to 6, yet sensitivity testing is usually done on agar at pH 7.2 to 7.4; thus, antibiotics that have considerably greater activity at alkaline pH, such as kanamycin and streptomycin, will appear to be far more effective on the agar test plate than they will be in the urine (at pH 5.5)—unless alkali or azetazolamide is given to raise the pH of the urine. Conversely, those substances

which are more effective at an acid pH, such as the tetracyclines and nalidix acid, may appear to be ineffective against a given organism on the test plate at pH 7.2 whereas in acid urine they might be quite effective.

These considerations are good reasons for microscopical and bacteriologic examination of urine about 24 hours after initiation of therapy for urinary-tract infections, to ascertain if drug resistance as determined in the laboratory is related to the therapeutic response. It is also reason to consider testing urinary-tract pathogens in mediums at different pH's as has been recommended and shown to be worthwhile, especially when medication to adjust the urine to the appropriate pH is also given.

Acquisition and Loss of the Drug-Resistance Trait

Bacterial cultures that show resistance to a given drug on laboratory testing generally give the same result if the test is repeated many times. However, a proportion of the cells in many cultures will lose the resistance trait with each passage in antibiotic-free medium, and a fraction of many drug-susceptible populations may acquire the resistance trait under special circumstances.

Although the appearance of heritable drug resistance in a previously susceptible strain was originally thought to be due to a spontaneous gene *mutation,* occurring about once in every 10^5 to 10^{10} cells, it is now known that determinants for the resistance trait may also be acquired by staphylococci by two other mechanisms: transformation and transduction. Many gram-negative bacilli may acquire the determinants by any of these three mechanisms or by a fourth one: conjugation. The last three mechanisms transmit "infectious drug resistance" although the term is mainly applied to that transmitted by conjugation. *Transformation* is the process by which a cell incorporates from its environment one or more genes formed by another cell. In *transduction,* genes formed by another cell are also incorporated into a recipient cell, but they are introduced by a temperate bacterial virus (one that does not lyse and kill its new host) along with its own genes. In *conjugation,* the genes to be transferred are cytoplasmic in location, and replicate independently and more rapidly than the bacterial donor cell and its other genes on the bacterial chromosome; conjugation, a form of bacterial sexual mating, may occur between cells of different species, and the genes determining drug resistance (R factors) are introduced (presumably via a "sexual pilus") into appropriate recipients by donor cells that possess the resistance-transfer factor (RTF). Transformation is a rare event, occurring perhaps once for every 10^8 cells; transduction may occur once for every 10^3 to 10^6 exposed cells, whereas in conjugation from less than 1 in 10^2 to virtually all properly exposed cells may acquire the new genes within a few minutes to an hour.

In gram-negative bacilli, acquisition of resistance to as many as seven drugs simultaneously has been reported, whereas in staphylococci, acquisition of resistance to one drug at a time is the rule. Similarly, the simultaneous loss of multiple-resistance determinants is the pattern in many gram-negative bacilli whereas, in staphylococci, such genes are lost individually. There is considerable variation in the spontaneous rates of loss of these genes and reversion to drug sensitivity. In salmonella species the R factors are least stable and may disappear from 25 percent of the cells per passage, whereas in *Escherichia coli,* shigella species and *Staphylococcus aureus,* rates of loss affecting one cell in 10^3 are often noted.

No clinically practical suggestion for accelerating this loss of resistance phenomenon has been made. Acridines and heat accelerated such loss rates in laboratory studies of some strains, but the majority of the bacterial populations were still drug resistant.

Mechanisms of Resistance

Penicillins and cephalosporins are hydrolyzed to inactive derivatives by enzymes produced by most organisms that are highly resistant to them; some gram-negative bacilli and methicillin-resistant strains of *Staph. aureus* have "intrinsic resistance" that is independent of penicillinases. Chloramphenicol, streptomycin, kanamycin and neomycin are inactivated by enzymes from resistant organisms by acetylation, phosphorylation or adenylation. Resistance to tetracyclines and isoniazid may be due to exclusion of drug by bacterial membranes.

Clinical Importance of "Infectious Drug Resistance"

Although many species of drug-sensitive pathogenic organisms can be changed to drug-resistant organisms in the laboratory, the extent to which this happens in patients has not been determined. Such conversion has been produced in animals, but the conditions required for such gene transfer probably rarely exist in human beings. Residence in a hos-

pital and treatment with any antibiotic will increase the frequency of antibiotic resistant organisms, either by the selection of resistance traits already present in organisms carried by incoming patients or by something new acquired from the hospital environment by those incoming patients—that is, either organisms already drug resistant or resistance genes that convert the sensitive organism they brought with them to a state of drug resistance. If either of the latter possibilities exist, a review of the feasibility of isolating new patients from such contamination may be in order. Although the search for new drugs has, to some extent, successfully kept pace with the emergence of drug resistance, there is no guarantee that this progress will continue.

I am indebted to Dr. Maxwell Finland for helpful suggestions in the preparation of this article and to Dr. James N. Wilfert. A. Kathleen Daly and Alice MacDonald for the information used in the tables.

(The references may be seen in the original article.)

CHRONIC FACTITIOUS ILLNESS

MUNCHAUSEN'S SYNDROME

Herzl R. Spiro, MD, Baltimore, Arch Gen Psychiat 18(5):569–579, May 1968.

Factitious illness is the appropriate diagnosis in patients who consciously distort their medical history and produce misleading physical findings and laboratory results through self-inflicted lesions. By simulating patterns of physical disease, these patients may cause themselves to be subjected to painful and dangerous diagnostic and treatment procedures.

"Munchausen's syndrome" represents a special pattern within the group of factitious illnesses. It is characterized by marked chronicity and the tendency of these patients to wander from hospital to hospital and city to city. Bean describes those afflicted with the syndrome as follows:

At the frayed end of . . . (the human) spectrum is the fascinating derelict, human flotsam detached from its moorings, the peripatetic medical vagrant, the itinerant fabricator of nearly perfect facsimile of serious illness—the victim of Munchausen's Syndrome.

Terminology.—The terminology used in describing this disorder is better noted for its color than its clarity. Asher not only proposed the somewhat facetious "Munchausen's" label, but he also proposed a series of subcategories: "laparotomophilia migrans," "haemorrhagica histrionica," and "neurologica diabolica." To this pseudo-scientific colorful appellation, Chapman has proposed two additions: "dermatitis autogenica" and "hyperpyrexia figmentatica." The nomenclature is perhaps symptomatic of the mixture of bemusement, bewilderment, contempt, and anger that these patients arouse in their physicians. Baron Hieronymus Karl Friederich von Munchausen (1720 to 1791) was a real character who wandered from city to city and from tavern to tavern telling tall tales. Another picaresque German confabulator, Rudolph Eric Raspe, published a volume purporting to tell of the Baron's adventures. The volume itself was a hoax, a product of Raspe's imagination. Some have suggested that the good Baron would have regarded the naming of this syndrome after him with the same displeasure with which he viewed Raspe's fabrications and incursion into his privacy. Frankel suggests that by giving the illness the name Munchausen's syndrome, one might be induced to regard these people simply as tricksters, liars, and swindlers. Small agrees that while the name is an imaginative one, more impersonal nomenclature might be more descriptive and meaningful. The name suggested by Clark and Melnick, "Hospital Hoboes," offers some of the dash and color of Munchausen's syndrome, but adds little in the way of descriptiveness or objectivity. Barker's term, "Hospital Addiction," is more descriptive, but we doubt that this syndrome is phenomenologically or dynamically similar to addiction. We would like to propose that all of these patients should have a primary diagnosis which is psychiatric. The underlying basis for the disordered behavior should be sought, and the neurotic, psychotic, or characterologic illness specified. Malingering should only be diagnosed in

Submitted for publication Nov 29, 1967.
From the Henry Phipps Outpatient Service, The Johns Hopkins Hospital, and the Department of Psychiatry. The Johns Hopkins University, Baltimore.
Reprint requests to The Johns Hopkins Hospital, Baltimore 21205.

the absence of psychiatric illness and the presence of behavior appropriately adaptive to a clear-cut long-term goal. The diagnosis could contain the qualifying phrase "with chronic factitious symptomatology." *Webster's International Dictionary* (second edition) defines factitious as follows: "Made by art, in distinction from what is produced by nature; artificial, sham . . . that is factitious which is brought about or wrought up by labor and effort." While rather drab and colorless compared to some of the other suggestions in the literature, the phrase, "with chronic factitious symptomatology" provides a more descriptive, nonepithetical appellation.

Although this syndrome has been known for at least 16 years and the possibility of serious emotional illness has long been recognized, the psychiatric literature contains but three reports. In no case is a detailed psychiatric work-up with a complete psychiatric history provided. Barker reviews seven cases in phenomenologic terms and notes the inadequacy of current knowledge concerning pathogenesis and etiology. Vail's report is primarily concerned with a patient's behavioral pattern during a brief stay in a state hospital. Bursten bases his perceptive report on two interviews with an "indignant," uncooperative patient seen on a medical ward, and he forthrightly expresses doubt about the reliability of the history. The paucity of psychiatric literature may not seem so surprising in view of Grinker's observation that there are only 12 documented case studies of any form of imposture in the psychiatric literature. In this paper we will review the medical literature on Munchausen's syndrome in order to draw a composite picture of the syndrome, and we will present detailed material on a patient seen for 45 hours of psychotherapy. In order to correct for the historical inaccuracy inherent in this disorder, we arranged separate interviews with the patient's wife, mother, and five of his nine siblings. Furthermore, we examined records concerning 39 hospitalizations and 14 additional emergency room visits. The results of psychometric testing after five year follow-up information are also presented.

Review of the Literature

The medical literature contains 38 cases of chronic factitious illness—25 men and 13 women. The ages range from 23 to 62. Much of the literature is concerned with the drama and the variety of the feigned medical illness. Many patients are described several times and one attracted 16 reports. The presenting complaints may be briefly summarized as follows: abdominal pain or vomiting, or both, nine cases; dramatic bleeding or anemia, eight cases; neurologic manifestations, ten cases; dermatologic manifestations, five cases and cardiac symptoms, five cases. The presenting symptomatology offers no real help in establishing the psychiatric diagnosis or prognosis. Many patients have suffered from a major organic illness at some earlier time. See Bagan for a medically oriented literature review.

Once hospitalized, the patient with chronic factitious illness is rarely quiet or cooperative. In 14 of the 15 cases in which behavior on the ward is described, truculence, evasiveness, and hostile behavior are specifically mentioned. Even prior to exposure these patients do such things as accusing staff members of theft, hurling china sputum mugs at nurses, and threatening physicians with violence and mayhem! After discovery, the most common behavior pattern is signing out against advice. This is specifically noted in 20 cases.

Several authorities decry the judgmental approach applied to these patients and the failure to obtain psychiatric consultation. None of the reports offer detailed life histories. Only 16 of the 38 patients were even seen by a psychiatrist. Where psychiatric consultation is reported, the following diagnoses are listed: psychopathic personality disturbance (five cases); schizophrenic reaction (three cases); other psychoses (two cases); other neuroses, primarily hysteria (five cases); no psychiatric illness (one case).

Seven of 13 female patients and nine of 25 male patients were seen by a psychiatric consultant. The most common diagnosis among the female patients was hysteria, with only one women being labeled a psychopath. The pattern is the opposite among male patients, with four being labeled psychopaths, two schizophrenics, and none being considered hysterics. In eight cases, psychiatric hospitalization is reported to have taken place. All three patients diagnosed as schizophrenics were placed in state hospitals at one time or another.

Impostureship is common in this disorder and is specifically described in seven cases. Four of the English patients pretended to have been war heroes and often claimed to have suffered severe wounds in battle. A prostitute from Picadilly identified herself as a Texan. A former drug addict, feigning purpura, claimed to be a priest on his way to a monastery. The colorful, blood-bespattered hero

of Chapman's Homeric saga variously presented himself as a professional wrestler, a claims' collector, and a merchant seaman who had traveled all over the world.

Motivating factors receive little consideration in the nonpsychiatric literature on Munchausen's syndrome. Some motives mentioned are as follows: (1) a wish to be the center of interest and attention in the dramatic role of patient; (2) a grudge against doctors and hospitals; (3) a desire for free board and lodging; (4) a need for a haven from the police; and (5) an addiction to drugs. In none of the patients are drug withdrawal symptoms reported. The need for far more information concerning motivation has been emphasized.

Thus, a review of the literature on this syndrome provides rich material concerning phenomenology and some speculation concerning motivation. In view of the absence of detailed historical material and psychiatric observations, we offer the following case.

Report of a Case

A 30-year-old, married, white, unemployed Catholic American-born male first came to psychiatric attention when he requested admission to the Henry Phipps Psychiatric Clinic of the Johns Hopkins Hospital five years ago. The presenting problems, as seen by the patient, were the following: (1) frequent hospitalizations for factitious complaints, (2) inability to hold a job, (3) very frequent lying and imposture, and (4) heavy alcohol intake. The patient stated that hospitalization was sought at that time because of the birth of his daughter, intensifying his desire to change.

The difficulties had been present since the patient's military service at age 18. He had suffered from abdominal pain and had been given a complete medical work-up. Nothing was found to be physically wrong with him, but subsequently he was discharged on grounds of unadaptability. The patient sharply differentiated the pain at that time from the pain which he feigned on later occasions. The former was quite real to him, though no organic pathological condition was established.

After discharge from the army, the patient drifted from job to job for three years. At age 21, he was admitted to a Baltimore hospital with typical renal colic and gravel was found in his urine. He stated that this was the only time that he was *not* feigning the pain of renal colic. Review of the hospital chart established that this was a true episode of ureteral lithiasis. Soon after discharge he married his first wife. He lived with this woman for 3½ strife-filled years. His employment was reasonably steady, but he did begin to go out with other women before the separation and he started to drink heavily.

He could not recall the first time that he was hospitalized with feigned complaints, but believed this occurred at age 24 (1955), after the breakup of the first marriage. He had had several checkups for nonfeigned functional abdominal pain with no positive findings. He then arranged to have himself hospitalized by feigning the typical pain of the left-sided renal colic and placing blood from a fingertip pin prick in his urine. A careful check with all the hospitals in the Washington-Baltimore area was made with the cooperation of the patient and the patient's second wife (who had saved all his Blue Cross receipts). It was established that the patient sought hospitalization 53 times before he reached age 30 and was admitted 39 times.

The patient married his second wife in 1955. The patient's wife had been married previously to a man who could not hold a job and whom she had supported. She was convinced that the patient would be a steady worker. Since their marriage in 1955, the patient had never held any job for more than 11 months. He had held such miscellaneous jobs as a sales representative, ice cream salesman, sheet metal worker, private detective, milkman, bill collector, medical investigator for the city pathologist, barkeeper, etc. He usually left jobs, either by quarreling with his superior or going on an alcoholic binge and being fired.

The patient's drinking behavior is of particular interest in that it is accompanied by another form of imposture. He generally installs himself in some bar and regales the patrons with stories from his experience as a physician, as an intrepid private investigator, or as a famous criminal lawyer. He tells these stories so convincingly that he is rarely discovered to be a fraud; however, he sometimes terminates the evening's activities by revealing his fraudulence and laughing at the bar patrons for their gullibility. Several fist fights have resulted.

These binges go on for several consecutive nights. When they are over he allegedly feels so ashamed that he cannot face his wife at home. He, therefore, goes to one of the local hospitals with the pattern of complaints described above. Because of these complaints he has had innumerable intravenous pyelograms (IVPs), several cystoscopies, and an

exploratory laparotomy. Many of the hospital charts carry a presumptive diagnosis of renal colic with no record of the factitious nature of the complaints being recorded. His behavior in the hospital is angry and demanding. On the occasions when the patient has been exposed, he has signed himself out of the hospital immediately. On reaching home, he dissolved in tears before his wife alleging remorse. Each time his wife stated that if this ever happened again, she would throw him out of the house. However, the marriage continued until after the psychiatric hospitalization. Little seemed to pass between them except recrimination and apology for the patient's asocial behavior.

The hospitalization leading to this report was precipitated by the birth of a daughter to the patient. On the evening of the daughter's birth, the patient went out and became drunk and then started a fight with several college students who refused to toast his daughter properly. He was in his criminal lawyer pose that night and became very angry when proper deference was not shown. Later on, in a fury, he rammed into the side of their car and was arrested for criminal assault. Trial for this charge had been deferred on several occasions. The patient had also been in trouble with the law for several moving traffic violations.

On the day of admission he was in Traffic Court. The fine was suspended when the patient informed the judge in a tone of great remorse that he intended to get psychiatric treatment and become a good father to his newborn daughter. The judge, apparently, informed the patient that he had the option of going to jail or getting psychiatric help. The patient followed his well worn path to the hospital doors and sought admission.

Past History.—This patient was born the second of ten children. He was a heterozygous twin, born full-term at home after a difficult breech presentation. Despite this, the patient's mother, who was interviewed in detail, recalls no stigmata of birth damage. His older brother was 15 months when he was born, and the patient's twin was a girl. A fourth child was born just 15 months after the patient. Thus, at one time the mother had four children in diapers. The patient's father was a baker; he was home a great deal during the day and tended to his own bake shop at night. He disciplined the children infrequently and often tried to prevent the mother from striking the children when she was angry.

The patient's mother sees herself as having been underindulgent. She regarded the patient as her favorite son because he was "such a good-looking, smart little boy." The patient's siblings and the patient concur that he was a favorite child, but do not see the mother as having been particularly overindulgent. She was a quick tempered woman who would beat the children with a large stick occasionally and with her hands frequently. The discipline, even in the earliest years of childhood, was very inconsistent.

The patient was bottle-fed and weaned at the age of 9 months with difficulty. Toilet training was begun before age 9 months with a rigid, mechanical routine, but voluntary control was not achieved until after the age of 3 years. Rhythmic head banging against the mattress during the night was frequent. The mother recalled that there was no time for her to take the children outside, so she would dress the four of them in winter clothing and place them next to an open window for a "daily airing."

When the patient was 4 years old, he was struck by an automobile and was hospitalized for two months with compound fractures of both legs. During this period he was kept in casts and traction on an adult ward. He recalled his stay in the hospital as having been very pleasant, particularly the large amount of attention he received from the professional staff, the other patients, and his own family. His earlies memories concern attention from the parents during the hospitalization. The mother states that the patient was in considerable pain during a good part of the hospitalization and was subjected to numerous stressful manipulations. The patient recalled none of this and insists the whole experience was a happy one. Soon after his discharge from the hospital, he developed mastoiditis and had to be rehospitalized. Then he developed measles and was transferred to still a third hospital for two more weeks.

There was a prolonged period during which the patient was semi-invalid learning to walk. At home he became much more of a problem to his parents, demanding attention and "acting up" when he did not get it. He entered parochial school at the age of 6 or 7, but he did not apply himself to his work and flunked one year. The patient's mother states that whenever he got into trouble, he would simply look up at her, smile, and say he was sorry and everything would be okay. She said, "I guess it's all my fault for not punishing him."

She recalls one occasion when he got into trouble in school and the teacher forced him to stand up for a long period of time. That night he compained of

cramps in his legs, and his mother sat up massaging him. The next morning she went in and bawled out the teacher for mistreating her son. Curiously, the patient's memory of this incident is quite different. He recalls that he got no support from his mother and was spanked for being a bad boy in school. He states that whenever he got into trouble he was whipped at home.

When the patient was just 10 years old, his father, then 38, had a coronary occlusion. He survived the first attack, but a week after he came home, he developed chest pain and went into congestive failure. The patient observed all this happening and was with his father as the doctors worked over him. Within less than an hour, his father died.

The patient states that, subsequently, the family "fell apart." The mother went to work at a cafeteria, working the hours of 6 p.m. to 1 a.m. The patient became very disobedient, rebelling at almost anything he was asked to do. After two years of repeated truancies, he was entered in a vocational school where he was trained to be a sheet metal worker.

When he was 14 years old, his mother remarried. The stepfather was a kindly but passive man who was dominated almost completely by the mother. Soon after the marriage, the patient and his mother had an altercation. The stepfather intervened, slapping the patient across the face. That day the patient ran away and joined the army.

The patient claimed that his record during this first tour of duty was spotless. This enlistment ended when at the age 15½ he had his mother tell the army he was underage. It is of interest that the patient's mother knew where he was during his entire period in the army. His stepfather wanted to have him sent home, but the mother replied that the experience of travel would let him get the "devilishness out of his system." She stated to the therapist that she had always wanted to travel herself, to see the world, and to "live it up," but had been prevented from so doing by her parents. She would not inflict the same thing on her son.

On his return home, the boy worked for a year in a bakery. Then he reenlisted in the army. This time he found that he could not stand being ordered around. He was frequently late for duty. He and his older brother were stationed in the same area and they could not get along. It was then that the stomach pain began.

Examination.—The patient was a tall, blonde, pleasant-looking man who displayed a great deal of superficial charm and an easy manner. The affect was bland with occasional outbursts of intense anger after therapy had proceeded for several weeks. Overt anxiety was betrayed only once (see below). Cognitive function was intact with no evidence to suggest a schizophrenic disorder. Physical examination, neurological examination, serologic test for syphilis (STS), and serial electroencephalograms revealed no abnormalities. Psychological tests including the Wechsler Adult Intelligence Scale (WAIS), the Bender Gestalt, the Rorshach, the Thematic Apperception Test (TAT), and the Minnesota Multiphasic Personality Inventory (MMPI) add little information. The patient showed a full scale intelligence quotient of 109 with minimal scatter. The verbal facility was *not* reflected in the test results. No evidence of psychosis appeared in projective tests results. The MMPI was consistent with a diagnosis of sociopathic personality disorder.

Hospital Course.—Initially the patient was quite hostile in his manner and repeatedly insulted ward personnel. He poked fun at other patients, upsetting several disturbed schizophrenics in a seemingly purposeful manner. He was manipulative but pleasant toward the therapist.

A turning point in therapy came when the patient smuggled a bottle of liquor into the ward, became slightly inebriated, and attempted to escape. When his flight was interdicted, he appeared somewhat anxious. The content of the following hours was entirely related to the hospitalization at age 4.

Discharge plans were complicated by the tremendous discrepancy in what the patient wanted and expected for himself and what he felt capable of doing. Here he was with the equivalent of a fourth grade education and with the aspirations of a man who had done six years of postgraduate work! A job was finally arranged which offered a good chance for advancement within the patient's limits. At the time of discharge from the clinic, the patient was getting along well with other patients on his ward, seemed to have curbed his impulsiveness, and was getting along reasonably well with the nursing staff, who noticed a marked change in his behavior. He was in a stage of strong positive transference toward the therapist.

On the other hand, he was quite alienated from his mother, sisters, and brothers. They were disgusted with him for behavior which went far beyond the bounds of amorality accepted in this rather asocial family. Strangely, they seemed to withdraw support as the patient moved toward a more stable adjustment. His wife and in-laws had been support-

ing him and were equally disgusted with him. The wife was clinically ill herself, manifesting signs of a chronic depression. She was seen several times together with her husband, but she refused to consider any treatment for herself. She had been adjusted to the role of martyred wife who reprimanded the psychopathic husband, and she too seemed upset by the patient's superficial improvement.

Subsequent Course.—For six months after discharge the patient continued to see the therapist on a weekly basis. The discussions centered on the anger at the family. Joint sessions with the wife were characterized by her complaints that "two babies" in the family were too many. The patient felt that neither the employer, the wife, nor the therapist were caring for him adequately. He shifted to a construction job to earn more money. Within a few months he sustained a back injury and dropped out of treatment. I learned that the patient had a laminectomy for a herniated nucleus pulposus and had collected a significant sum from Workmen's Compensation soon after leaving therapy. The patient then returned to his peregrinations from hospital to hospital shifting his pattern from renal colic to abdominal pain and "hematemesis."

One year later, I was called by a besieged surgeon who had done a partial gastrectomy and was in difficulty with a hospital tissue committee. Subsequently the patient separated from his wife. Dissemination of information to local hospitals had only resulted in wide geographic excursions. The family now believes he is in the environs of Denver, still afflicted with the illness that brought him to psychiatric care.

Comment

The boundaries between hysteria, factitious illness, and malingering are ill defined. Supposedly, the patient with factitious illness is capable of conscious control and the behavior is backed by full conation and volition, in contrast to the hysteric whose symptoms are a product of the unconscious. Because of the alleged availability of willful control, the patient with Munchausen's syndrome is subject at best to derisive humor and often to scorn and anger from his physicians. Symptoms which stem from voluntary, conscious acts of malice do not place one within the pale of the "true" patient role.

Manager: Will you oblige me by going away? We haven't time to waste with mad people.

The Father: Oh sir, you know well that life is full of infinite absurdities, which, strangely enough, do not even need to appear plausible since they are true. . . . We . . . have no other reality outside this illusion.

Like Pirandello characters, those with chronic factitious illness find themselves locked in a blurred play where real life and acting are indistinguishable. Where does the play stop? What appears to the casual observer to be "the play" slips beyond the control of the patient. True, he knows when he is "acting" (unlike the hysteric), but even with this knowledge *he can not stop acting,* as is well illustrated in this patient's history. This feature differentiates most patients with chronic factitious symptomatology from malingerers.

As with the compulsive wanderer, the impostor, the drug addict, and the alcoholic, seemingly willful acts are determined by unconscious factors and environmental cues to produce a psychiatric illness of profound dimensions. The failure to see this as an illness may provide the external milieu in which the illness thrives. The masochism must be well served by the angry tirades from irate medical personnel and the stage set for the next episode. The illness is partly iatrogenic, for it requires more than one party to produce a sadomasochistic relationship.

The superficial motivational factors summarized above in the literature review are not a sufficient explanation for this disorder. Desire for bed and board, desire for drugs, escape from legal punishment, and the desire to be the center of attention represent reclassification of phenomenology rather than dynamic formulation. We will discuss the syndrome first in terms of the usual psychiatric nomenclature and then in terms of the dynamics of the features peculiar to this illness.

The nature of the psychiatric illness most likely varies from patient to patient. Just as psychogenic pain may be caused by a depressive reaction, a conversion reaction, a psychophysiologic reaction, or the somatic delusional system of schizophrenia, factitious illness may be symptomatic of several psychiatric disorders.

The schizophrenic pattern is well illustrated by Chapman's celebrated patient who received a full psychiatric evaluation during his stay at Johns Hopkins. We see little point in rereporting the case of a patient whose history is already contained in seven publications. Suffice it to say that there was clear-cut evidence of a cognitive disorder and a paranoid delusional system. The records of the state hospital to which he was sent confirm this conclusion. Vail reports a similar case of well-established schizophrenia. Burstein's statement concerning the ab-

sence of a thought disorder is not true for all cases and the underlying illness may sometimes be schizophrenia. Self-mutilation among psychotic patients is not uncommon and the dynamics of such self-mutilation may shed light on the causes of factitious illness.

Hysteria is often cited as the underlying illness in reported cases (see above). As Bursten points out, the intense affective involvement in the complaints, the conscious falsification (even though unconsciously determined), and the absence of the usual features of the hysterical character cast doubt on the use of this diagnosis. Attempts at mutually exclusive categorization may be unwise; several patients in our files who have documented acute factitious illnesses have *also* had episodes of conversion neuroses. Even the chronic patient reported herein suffered what appeared to be conversion abdominal pain on several occasions. The relationship between factitious and hysterical symptomatology is not a simple one of exclusion or inclusion. Patients with one predominant pattern (hysterical or factitious) may manifest the other pattern episodically. The dynamic factors in hysterical and factitious symptomatology may bear some similarities.

The sociopathic pattern of factitious illness is well illustrated by our patient. Like many sociopaths he manifested glibness, evasiveness, poor impulse control, some difficulties with the law, and minimal evidence of guilt or anxiety. This is in accord with numerous other case reports. Unfortunately, the shift from a diagnosis of "Munchausen's Syndrome" to "Sociopathic Personality Pattern Disorder with Chronic Factitious Symptomatology" may represent a leap from frying pan to fire in terms of name calling and epithets! On the other hand, the shift involves the use of a diagnostic category which involves some objective study, infrequent though this may seem. Thus, the concept of acting out, well summarized by Greenacre may be useful. The studies of Jenkins and Johnson and Szurek are also revealing.

Jenkins states that sociopathy may be related to inconsistent discipline, paternal rejection, and the development of negative attitudes towards the mother. Our patient's early childhood situation must have fostered a great deal of resentment and bitterness. The patient's mother was an inconsistent woman whose punishments were largely dependent on mood. There was gross unpredictability in the child rearing situation. The mother fought the school, condoned vandalism, and let her son run away to the army. The marked discrepancy between the formal and emotional responses are similar to the cases cited by Johnson and Szurek. The mother's satisfaction in the son's acting out is blatantly manifest in the interviews with the mother.

Any effort at understanding this illness must go beyond psychiatric nomenclature to deal with the dynamics of several features of the illness: (1) The posing, impostureship, and pseudologia fantastica found in such patients. (2) The choice of the medical facilities as the rightful stage upon which to enact the fantastic roles and masochistic scenes. (3) The rootless, wandering lives of these unfortunate people; the chronic homeless peregrination and absence of longstanding close relationships. (4) The masochistic perpetration of self-injury and acceptance of painful or even dangerous procedures.

1. The cases reviewed led themselves to particular attention in the light of the literature on impostors. Several writers have noted that factitious disease in and of itself represents a form of imposture, for the patient poses as being severely and dramatically ill. The medical literature showed clear-cut cases of false role assumption in addition to the sick role. The area of congruence between factitious disease and impostors goes beyond mere phenomenologic similarity to three areas of dynamic interest: (*a*) history of early deprivation; (*b*) the discrepancy between ego ideal and self-image; and (*c*) mastery over early traumata.

Preoedipal deprivation is emphasized by Abraham as an etiologic factor in his case report of an impostor. Berglar also emphasizes the unconscious need to inspire love and admiration as well as the wish to obtain revenge upon the frustrating pre-Oedipal mother. For all the difficulties in obtaining accurate histories concerning the pre-Oedipal period, one is hard pressed to escape the conclusion that our patient's early life was characterized by relative neglect. The mother had four babies in diapers simultaneously. Walks outdoors were replaced by airing next to an open window. We also know that both weaning and toilet training were enforced by an inconsistent, somewhat brutal mother in a mechanical way very early in development. One might view this early deprivation as a sensitizing experience making the patient more susceptible to the later traumata.

Related to the analytic view concerning early deprivation is the incomplete ego development and distorted body image (particularly with regard to fancied defective genital development) postulated by Greenacre, as well as the discrepancy between ego-ideal and self-image postulated by Deutsch. Bursten has related these dynamics of the impostor to the

patient with chronic factitious illness and we are able to confirm his findings. Our patient's grandiose aspirations and fourth grade education mixed poorly. The pattern of sexual activity was suggestive of those men with doubts concerning genital adequacy. The repeated cystoscopy not only in our patient, but also in several other reported patients, is not unrelated.

Of the formulations concerning impostors, Grinker's concept of mastery seems by far the most useful and applicable to factitious illness. Grinker reports a case of an impostor who described events that had occurred three years previously as if they were occurring during the same years that the therapy was taking place. This is interpreted as representing a form of mastery of earlier traumatic struggles and frustrations. There is the seeking of love and approval from the new object, as well as revenge through superiority and hostility expressed by the knowledge of the deception. The traumatic incident is clear in our patient's case. At age 4½ he is hospitalized after an automobile accident. He remains hospitalized, immobilized in cast and traction, and subjected to painful manipulations and procedures for the better part of one year. The unpleasant aspects of this experience, so clearly recalled by family members, are repressed by the patient. The hospitalization is recalled as a triumph for his verbal virtuosity; he obtained "a place in the sun" as the center of adult attention.

Now in adult years, the patient remasters the pain and fear over and over again. He elicits once more the intense if ambivalent attention of "adults" by demanding behavior in the spurious role of patient. This time the patient can engage in flight at will. Grinker's concept is particularly useful in that it extends and incorporates the early concepts of preoedipal deprivation, body image distortion, and ego-ideal self-image discrepancy.

2. Selection of the hospital as the stage for the drama of posing, masochism, and flight is a second factor to be explained. The dynamics of the phenomenon of imposture may shed light on the choice of the patient role. As we have noted, early experiences with illness and hospitalization represent the traumata to be reenacted and mastered. Thus, the hospital becomes the arena. Blumer has found that patients with chronic functional pain syndromes often report critical experiences with illness in themselves or their parents. Once more we find similar historical factors in conversion and factitious symptoms.

Features of the doctor-patient relationship also bear on the role-choice. The "doctor game" was interpreted by Simmel as related to oedipal turmoil. Granting the continual relevance of the sexual-seductive aspects of childhood precursors of the "doctor game," we wonder whether modern medicine has not introduced its own current problems. Our "scientific" medical care system involves aspects of alienation, dehumanization, and pseudo-caring which may represent significant dynamic factors in factitious illness.

The selection of disease and hospitalization as the focal area for reenactment is thus explained. The patient with factitious symptoms seizes control of the illness. He creates the illness and thus he can terminate it. Occasionally he loses control of matters and submits to surgery. This latter point requires further elucidation and must be related to the masochism. Ultimately control is reasserted when the patient walks out of the hospital against medical advice.

3. What impels the restless wandering of these patients? Increasing notoriety in the Baltimore-Washington area left our patient little choice. The broken record reiteration of childhood trauma called for new hospitals and new cities. Yet such a rootless, friendless life involves such a rupture of usual object relations that we wonder what psychopathologic factors may be involved.

Stengel's description of compulsive wanderers may bear on this phenomenon. More than half of his cases also manifest "compulsive pseudologia" suggesting that impostureship, peregrination, and factitious illness may be closely related. Furthermore, Stengel describes the early childhood as manifesting emotional distance and interprets the wandering as a search for the lost primary love objects. In chronic factitious illness medical facilities seem to substitute for significant childhood objects.

True interpersonal intimacy seemed too threatening for our patient. The wandering was doubly dictated by the search for intimacy and the inability to accept such closeness.

4. The self-multilation, the painful diagnostic and therapeutic procedures, and the personal humiliation invited by these patients may be phenomenologically described as "masochistic." Bursten places this behavior in an intermediate position between sexual and social masochism. The concept of reversal of subject and object is invoked and speculation is offered that the patient truly identifies himself with the hostile, pain-inflicting physician. This specu-

lation seems close to the mark, for our patient, during his "bar stool impostureship," often selected the role of physician. His experience as a technician for the city pathologist rendered him quite familiar with medical matters. Contrary to Bursten's prediction, the paramedical role did not substitute for the factitiously produced patient role.

Does the theory of masochism offer anything else to our understanding of factitious illness? The concept of the death instinct and the concept of sadism turned against the self may represent interesting theoretical speculations, but contribute little to our understanding of this disorder. Several recent formulations of masochism emphasize the effort to maintain a close relationship with a sadistic primary love object. How could this explain the behavior of these "peripatetic wanderers" whose object relations are limited to a different angry head nurse each month?

Perhaps in this very behavior lies some further insight. The powerful impact of an aloof, hostile parent figure may persist and be dealt with in the guise of a rebellious yet masochistic relationship with a large institution (ie, a hospital). Our patient finds in the hospital the reward system which reenforces and perpetuates his behavior. In childhood, he left the deprivation of a mechanically run household crowded with diaper-clad infants to become the center of attention on a ward. The hospital, with its mixture of care and pain, of attention and fear, of dependency and rejection, is an effective substitute for this patient's mother, who mixed sadistic beatings with leg massages and doting love with bored rejection.

Still another question arises: how do these patients evoke and sustain the reactions described in the literature review? In an era of modern psychiatry, how does a symptom complex earn an epithet like Munchausen's syndrome instead of a legitimate diagnosis? In 22 of 38 cases of obviously disturbed behavior presented in journals, how does a psychiatric consultation come to be omitted? How do these patients induce their physicians to cooperate so fully in the antitherapeutic regime of painful and dangerous diagnostic and surgical procedures? In short, how do they achieve "narcissistic mortification" and humiliation? How do these patients succeed in subverting and sabotaging the well-intended efforts of well meaning, honest physicians?

The hostility of these patients is apparent. As summarized above, 14 of 15 patients exhibited obstreporous behavior. Indeed, the very impostureship involves the hostile duping of the physician. Perhaps physicians are ill disposed to respond charitably to such an assault on medical omnipotence and omniscience.

Summary and Conclusion

"Munchausen's syndrome" is a misnomer for a group of psychiatric illnesses manifest by chronic factitious symptomatology. We review here 38 of these cases in terms of the variegated, dramatic presenting features, the obstreporous behavior in the hospital, the paucity of psychiatric information, and the surface motives invoked as explanations in the nonpsychiatric literature. We present the first detailed psychiatric case study of this condition in the literature.

The psychiatric illness producing chronic factitious symptoms may be sociopathic, hysterical, or schizophrenic. Malingering alone is unlikely to produce such a severe chronic behavior disorder. The induced social field effects of the hostile dependent imposture are manifest in medical collaboration with a program of "antitherapy."

Impostors, functional pain patients, wanderers, and masochists show phenomenologic and psychodynamic similarities to patients with chronic factitious symptoms. Early childhood deprivation and difficult relationships with aloof, absent, or sadistic parents may sensitize the latter patients to distorted learning stemming from traumatic early illness or hospitalization. The concept of mastery as applied by Grinker to impostors offers the most useful explanation for the subsequent behavior.

(The references may be seen in the original article.)

LYMPHOMA OF THE COLON SIMULATING ULCERATIVE COLITIS

REPORT OF FOUR CASES

Henry B. Friedman, MD, Gary M. Silver, MD,† and Charles H. Brown, MD,*
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Malignant disease of the colon associated with ulcerative colitis is not rare. Because of the epithelial or mucosal destruction, regeneration, and replacement, the great majority of neoplasms associated with chronic mucosal ulcerative colitis are adenocarcinomas. The coincidence of adenocarcinoma of the colon and chronic ulcerative colitis has been reported by various authors as ranging from 0.2 percent to 11.1 percent on surgical specimens. In 1965, a review of 1258 cases of chronic ulcerative colitis treated from 1950-1963 disclosed only 22 cases of carcinoma, a 1.9 percent incidence of carcinoma of the colon associated with ulcerative colitis.

All studies and figures indicate that lymphoma of the colon associated with chronic ulcerative colitis occurs less frequently than does carcinoma; in a review of the literature in English we found reports of only 11 cases. Because this association is rare, we are reporting 3 cases of lymphosarcoma of the colon and one case of Hodgkin's disease of the colon, all of which at first appeared to be associated with chronic ulcerative colitis, but which instead were found to have mimicked chronic ulcerative colitis.

Report of Cases

Case 1. A 37-year-old man was first examined on Sept. 10, 1965. He had been having 10-20 loose, watery, and sometimes bloody bowel movements preceded by adominal cramps, daily for the past 8 years and had lost 20 lb. during this time. Physical examination was normal except for the presence of pulmonary osteoarthropathy. Proctoscopic examination to 10cm. revealed the rectal mucosa to be hyperemic and friable with circumferential ulcers and pseudopolyps. Abnormal laboratory data included an alkaline phosphatase of 54.6 K.-A. U.; sulfobromophthalein retention 12 percent in 45 min.; and serum carotene 25 μg./100 ml. Review of the roentgenograms of the colon, made at another institution 1 week previously, revealed shortening of the colon with small symmetric ulcers of the descending and sigmoid portions.

On the basis of proctosigmoidoscopic examination and roentgenograms of the colon, a diagnosis of chronic ulcerative colitis was made. Treatment was initiated with tranquilizers, vitamins, antispasmodics, bulk producers, hydrocortisone enemas, salicylazosulfapyridine, and adrenocorticotropic hormone (ACTH). When seen 2 months later, the patient had gained 14 lb. and was having three soft formed stools daily without pus or blood.

He was re-examined on Apr. 1, 1966, and at that time was icteric. The urine was dark. The edge of the liver was palpable from two to three fingerbreadths below the right costal margin. Proctosigmoidoscopic examination to 15 cm. revealed pseudopolyps, no ulceration or granularity, and only slightly increased mucosal friability. Hemoglobin was 12.9 mg./100 ml.; cell volume, 41 percent; total bilirubin, 2.9 mg./100 ml.; direct bilirubin, 1.6 mg./100 ml.; and alkaline phosphatase, 56.4 K.-A. U. The patient was admitted to the hospital on Apr. 24, 1966. A roentgenogram of the colon at that time revealed chronic ulcerative colitis affecting the entire colon, with possible neoplasm of the lower sigmoid. A scintigram of the liver revealed poor uptake of the radioactive gold (^{198}Au).

Laparotomy was performed, disclosing an annular lesion of the sigmoid, which would not admit a fingertip, and a loop ileostomy was performed. There were metastatic lesions in both lobes of the liver, biopsy of which revealed reticulum-cell sarcoma. Postoperatively, the patient was given cobalt-60 teletherapy (3000 R in 3 weeks) to the right upper and left lower abdominal quadrants, after which he was discharged from the hospital. The final admission on Mar. 8, 1967, was for hematemesis, which was treated successfully with a bland diet and hourly mild antacids. Six days after admission the patient had an unexpected seizure and died immediately. At autopsy, reticulum-cell sarcoma was found to involve the liver, the kidneys, and the pancreatic and mesenteric lymph nodes, as well as the colon. There were also superficial mucosal ulcerations of the colon. The central ner-

From the Department of Gastroenterology, The Cleveland Clinic Foundation, Cleveland, Ohio.
* Fellow, Department of Gastroenterology, Cleveland Clinic.
† Fellow, General Surgery, Cleveland Clinic.

vous system showed only anoxic changes in the cerebellum and microinfarcts in the right temporal lobe of the cerebrum.

Comment. This patient had had bloody diarrhea for 8 years, and had lost 20 lb. A diagonsis of chronic ulcerative colitis was made on the basis of proctosigmoidoscopic examination and roentgenograms of the colon. Only when operative intervention became necessary, because of unexplained jaundice and a possible neoplasm of the sigmoid colon, was the patient found to have reticulum-cell sarcoma of the colon with hepatic metastases, rather than chronic ulcerative colitis.

Case 2. A 54-year-old woman was first examined on June 6, 1966, because of numerous watery stools (6-8 per day) for the previous 18 months. In 1964, a laparotomy at another hospital for sudden diarrhea and abdominal cramps had revealed obstruction in the right colon; a right hemicolectomy and primary ileotransverse colon anastomosis were performed. The pathologic diagnosis of the excised specimen was chronic ulcerative colitis. Since her discharge from the hospital, the patient had noted a gradual increase in the number of bowel movements to eight per day, of increasingly loose, watery consistency, associated with abdominal cramps and the passage of much flatus.

Physical examination was within normal limits. Proctosigmoidoscopic examination to 18 cm. revealed absence of the rectal valves and narrowing of the lumen of the rectum and sigmoid colon. The mucosa was pale and granular, and bled easily.

A review of the roentgenograms of the colon taken elsewhere in January 1966, revealed narrowing of the distal portion of the colon with loss of haustral markings. On the basis of the history, the prior operative findings at another hospital, the proctosigmoidoscopic examination, and roentgenograms of the colon, a diagnosis of chronic ulcerative colitis was made. The patient was treated with a high-protein, high-carbohydrate, low-residue diet, tranquilizers, vitamins, antispasmodics, and a bulk producer. In addition, she received salicylazosulfapyridine, 2 tablets 4 times daily, hydro-cortisone enemas nightly for 12 nights, and ACTH, 40 units intramuscularly twice weekly.

In July 1966, review of the pathologic slides of the right colon removed 2 years previously showed malignant lymphoma of the colon with ulcerative ileitis secondary to obstruction. The patient was admitted to our hospital on July 24, 1966, for cobalt-60 teletherapy to the abdomen. A total tumor dose of 1800 R was administered over a 25-day period by "moving-strip" technic. Liver biopsy at this time was negative for metastases.

After the institution of medical management and radiotherapy, the diarrhea ceased, with only one or two soft formed stools daily. On Sept. 6, 1966, the patient was asymptomatic. A roentgenogram of the colon at that time showed the ileotransverse colostomy and no evidence of recurrent tumor. The colon was smooth with no haustral markings. No ulcerations were seen.

Comment. The patient underwent right hemicolectomy with primary ileotransverse colon anastomosis because of obstruction in the right colon after diarrhea of 18 months' duration. The pathologic diagnosis was chronic ulcerative colitis. Diarrhea continued after the operation, and 2 years later proctosigmoidoscopic examination and roentgenograms of the colon were interpreted as diagnostic of chronic ulcerative colitis. However, review of the slides of the resected colon showed not ulcerative colitis but malignant lymphoma.

Case 3. A 73-year-old man was admitted to our hospital on Mar. 30, 1956, because of bloody diarrhea and generalized abdominal cramps of 2 weeks' duration. His temperature was 101.5° F. and he appeared chronically ill. The chest was emphysematous with inspiratory and expiratory wheezes heard throughout the lung fields. The abdomen was diffusely tender; no organs or masses were palpable, and bowel sounds were active. Proctosigmoidoscopic examination revealed a mass that appeared to be a carcinoma 10 cm. above the anal orifice, on the posterior rectal wall. The pathologic diagnosis of two biopsy specimens varied between infected lymphoid polyp and chronic inflammation of the rectum. One week later the patient underwent a transverse loop colostomy. The colon was diffusely inflamed, resembling the appearance of chronic ulcerative colitis. The two days later, retention enemas of succinylsulfathiazole and penicillin were begun, and salicylazosulfapyridine was given orally.

The patient was discharged from the hospital on May 2, 1956, and readmitted 5 months later because of progressive deterioration with much rectal bleeding. Subtotal colectomy and terminal ileostomy were performed and a pathologic diagnosis of lymphosarcoma of the colon was made. After the operation the patient received cobalt-60 teletherapy (750 R) to each side of the abdominal cavity. On Dec. 29, 1956, he developed obstruction of the small

intestine, which was surgically decompressed. Pneumonia supervened and he died on Jan. 19, 1957.

Postmortem examination revealed radiation changes in the lymph nodes, spleen, and gastrointestinal tract; chronic suppurative peritonitis; microabscesses in the myocardium and kidneys; pulmonary edema and residual lymphoma in lymph nodes, spleen, and bone marrow.

Comment. The patient had lymphomatous involvement of the colon from the onset of the disease, yet the histologic patterns of two biopsy specimens of the rectum were inconclusive, and the colon at operation grossly resembled the appearance of chronic ulcerative colitis. A diagnosis of lymphosarcoma was made only after the entire colon was removed because of the progressive clinical deterioration of the patient.

Case 4. A 52-year-old man was first examined on Jan. 5, 1954, because of intermittent diarrhea of 11 years' duration, and intermittent abdominal pain in the left lower quadrant for 6 months. Physical examination was unremarkable except for the presence of left lower quadrant tenderness. Proctoscopic examination was normal. A roentgenogram of the colon showed inflammation of the cecum and ascending colon, consistent with amebiasis or ulcerative colitis. A graded-residue diet was recommended, with sedatives and antispasmodics, phthalylsulfathiazole, 1 gm., 4 times daily, and arsthinol, 5 tablets daily for 1 week.

The patient had only minimal pain in the left lower quadrant, and no diarrhea for the next 7 years. He was seen again on Sept. 15, 1961 because of intermittent pain on the right side of the throat, precipitated by swallowing. Examination revealed a lesion in the region of the right lingual tonsil, and a biopsy specimen showed reticulum-cell sarcoma of the base of the tongue. The lesion was irradiated with cobalt-60, a total tumor dose of 3600 R being administered; the lesion disappeared completely.

Thereafter, the patient was examined yearly, and roentgenograms of the colon showed chronic old right-sided ulcerative colitis. On Aug. 22, 1967, at his yearly examination, he still had intermittent crampy abdominal pain in the left lower quadrant. Abdominal examination now revealed the liver edge to be 1½ fingerbreadths below the right costal margin. Proctoscopic examination showed mucosal granularity. A roentgenogram of the colon now showed evidence of old chronic ulcerative colitis of the right colon with a constricting lesion of the midtransverse colon with overhanging margins, characteristic of carcinoma. A scintigram of the liver revealed decreased uptake of radioactive substance in the lower right lobe, consistent with a space-occupying lesion. The patient was admitted to the hospital on Aug. 24, 1967, and underwent subtotal colectomy and ileorectal anastomosis. The pathologic diagnosis was Hodgkin's disease of the entire right colon.

After operation, persistent hypertension and mental confusion developed. Blood pressures were as high as 230/140 mm. Hg. Hydroxyzine, 50 mg., was administered intravenously to treat the patient's mental confusion, and the blood pressure dropped to 90/60 mm. Hg, where it remained. Acute renal failure supervened, and the patient died on Sept. 10, 1967.

Comment. This patient had chronic ulcerative colitis, according to roentgenographic evidence, for 13 years. The roentgenograms of the colon showed progressive narrowing of the right transverse colon during a 6-year period after 1961. On the roentgenogram made this year (1967), this constricting lesion in the transverse colon was seen to have overhanging margins, simulating carcinoma, for the first time. This lesion appears to have been present, though much less prominent, on all of the roentgenograms of the colon since 1961. It is highly possible that from the onset of his symptoms he had Hodgkin's disease of the colon, rather than ulcerative colitis. One also wonders whether any relationship existed between the lesion in the colon and the reticulum-cell sarcoma at the base of the tongue, discovered 6 years ago and apparently completely eradicated.

Discussion

A number of reports suggest a relatively short survival in patients with lymphoma of the colon. Gechman *et al.* presented 1 case of Hodgkin's disease of the rectum and reviewed 11 other cases. All of these patients with Hodgkin's disease survived less than 1 year after the time symptoms of colonic obstruction developed. In the series of Allen *et al.*, the longest survival of patients with lymphoma of the colon was slightly over 2 years. Parkhurst and MacMillan reported a survival of up to 8 months in their series of patients with lymphoma of the colon.

In contrast, there have been a number of reports of patients in whom a clinical diagnosis of chronic ulcerative colitis was made originally but who subsequently were found to have lymphoma of the colon.

In many of these patients the onset of symptoms was many years prior to the diagnosis of lymphoma. In 1928, Bargen reported 2 patients with chronic ulcerative colitis, in one of whom lymphosarcoma of the cecum developed 40 years after the diagnosis of ulcerative colitis was made; in the other, Hodgkin's disease of the transverse colon developed. In 1947, Warren described 2 patients, both of whom had chronic ulcerative colitis for many years; in one, malignant lymphoma of the rectum and adenocarcinoma of the splenic flexure developed, and in the other, diffuse lymphoma involving the rectum developed. Since then, seven other similar isolated case reports have been published; all of the patients had chronic ulcerative colitis with apparent development of malignant lymphoma.

All of these patients had a history of cramping abdominal pain, fever, and bloody diarrhea. In addition, some had arthralgias, erythema nodosum, and a psychologic precipitating factor, all of which were suggestive of chronic ulcerative colitis. Roentgenograms of all these patients showed typical chronic ulcerative colitis, 3 with evidence of pseudopolyps. In all, the proctosigmoidoscopic examinations were interpreted as chronic ulcerative colitis. Only 1 patient underwent rectal biopsy, and the pathologic diagnosis was ulcerative colitis. All patients responded to medical treatment for periods ranging from 3 to 22 years, with an average duration of 13 years, until further symptoms necessitated laparotomy or until the patient died. At the time of laparotomy or necropsy, a lymphoma was found in each case.

It is questionable whether all of these patients had chronic ulcerative colitis that underwent "malignant degeneration" or, indeed, whether malignant lymphoma was present from the beginning; the roentgenograms, proctoscopic examination, and even the clinical course were misleading, closely resembling the picture of chronic ulcerative colitis. Federman and his co-workers believed that their patient had reticulum-cell sarcoma, rather than chronic ulcerative colitis, for the entire 15 years that they followed her progress. Two of the 4 patients in our series definitely had malignant lymphoma from the onset of their symptoms. The third patient (Case 1), originally thought to have chronic ulcerative colitis, on the basis of proctosigmoidoscopic examination and roentgenograms of the colon, had reticulum-cell sarcoma, found at laparotomy 9 years after the onset of his symptoms. The fourth patient in our series (Case 4) was believed, on the basis of roentgenograms, to have rightsided ulcerative colitis for 13 years, but was found to have Hodgkin's disease of the colon when laparotomy was performed for what roentgenographically appeared to be carcinoma of the colon.

The two disease entities (chronic ulcerative colitis and malignant lymphoma) may have similar clinical pictures, roentgenograms, and gross and microscopic findings, as evidenced by Case 3. The clinical picture, proctoscopic findings, and roentgenograms of the colon were similar to those seen in chronic ulcerative colitis. Two rectal biopsy specimens were interpreted as lymphoid polyp and lymphoid infiltration and ulceration, inconclusive for a diagnosis of malignant lymphoma. Only when the entire colon was removed because of failure of the patient to respond to medical treatment was a diagnosis of malignant lymphoma made. Therefore, it is questionable whether these 11 cases, to which the 4 cases of our report are now added, making a total of 15, represent chronic ulcerative colitis with subsequently developing malignant lymphoma, or whether malignant lymphoma was present from the onset, with the apparent clinical picture and the proctologic and radiologic findings of chronic ulcerative colitis.

While the clinical, sigmoidoscopic, and roentgenological differential diagnosis of lymphoma and ulcerative colitis is difficult, frequently the pathologic diagnosis is equally difficult, especially in areas of reaction proximal to chronic infection. With chronicity, the leukocytic infiltration in ulcerative colitis assumes a nonspecific mononuclear pattern because of the predominance of lymphocytes. The histologic pattern in malignant lymphoma consists of infiltration with round cells, usually of the same degree of maturity. The morphology of this type of cell very closely approaches that of the small lymphocyte. Fortunately, the incidence of lymphoma of the colon is infrequent. Perhaps the problem of lymphoma of the colon and ulcerative colitis will be comparable to that of gluten enteropathy and lymphoma of the small bowel in which some instances of each disorder are misdiagnosed as the other, and in which some patients appear to have both disorders.

Summary

Eleven cases diagnosed initially as chronic ulcerative colitis, and in which subsequently malignant lymphoma developed, have been reported since 1928. Four more such cases are reported here. It is postulated that all of these patients may have had malignant lymphoma at the onset of their symptoms, rather

than "malignant degeneration" of chronic ulcerative colitis.

(The figures and references may be seen in the original article.)

IMMUNOLOGICAL RESPONSE IN INFECTION

L. E. Cluff, MD, Amer J Med Sci 256:1–8, July 1968.

The immunological response to infection may be protective, harmful, or of no obvious consequence. In some instances, the protective effects of a particular immunological response are associated with injurious effects as well. For example, the response to pneumococcal capsular polysaccharide is associated with acquired resistance to infection, but the immune person will have an acute inflammatory reaction to polysaccharide injected into skin. Whether or not the effect will be harmful, protective or of no consequence appears not to influence the development of an immunological response to microbial antigens.

Immunology has contributed significantly to our understanding of bacterial variability, acquired resistance and the pathogenesis of infection. Nevertheless, immunologic processes are biologic mechanisms with broader implications and certainly are not peculiar to infection. From this point of view, the immunological responses to the complex antigens of microorganisms probably are little different than the immunological responses to nonmicrobial antigens. Therefore, microorganisms represent only one type of antigen to which human beings are exposed.

The differences between the immunologic response to infectious agents and other antigens are related to the peculiarity of microorganisms. Microorganisms have a complex antigenic structure. They replicate and are invasive. They vary in tissue localization and may have primary toxic or injurious effects. They have considerable antigenic variability and can mutate without complete alteration in antigenicity. In addition, some microorganisms may persist in the body for long periods of time, and can cause recurrent infection. Furthermore, antibiotics which disintegrate or facilitate lysis of microorganisms can affect the immunological reaction to the antigens of the parasite.

Replication of a microorganism during infection determines the antigenic mass which induces an immunological response. Generally, the smaller the antigen mass the smaller the immunologic stimulus and response. Under certain circumstances, however, unrestricted microbial growth might induce immunological tolerance or immunological paralysis.

Invasiveness is the usual but not invariable characteristic of a pathogenic microorganism, and the degree of invasiveness may significantly influence the immunological response in infection. For example, the tetanus bacillus is not invasive and tetanus antitoxin is never found in serum following recovery from the infection. If sufficient tetanus toxin was elaborated as a result of microbial growth to induce considerable immunological response, the patient would not survive. Similarly, the diphtheria bacillus ordinarily is not invasive, but sufficient toxin may be absorbed during the course of infection to induce considerable immunological response. In both these instances the immunological response is limited by the noninvasiveness of the infection and the toxicity of microbial extracellular products.

Some microorganisms are so invasive that death may ensue before an immunological response can develop, even though the antigenic mass is large. It might be predicted, therefore, that those infections in which immunological mechanisms may be responsible for manifestations of disease will be attributable to invasive microorganisms with moderate or low pathogenicity.

Obviously, the site of invasion by a microorganism may be the site of disease; for example, pulmonary tuberculosis following inhalation of tubercle bacilli and staphylococcal skin infection following invasion of the skin. In addition, dissemination of the organism or its antigens through the body can occur with different sites of localization. Certain infections localize in kidney, adrenal gland, joint or bone, while other microbes may localize in brain or skeletal muscle, and the different localization of microorganisms has important immunological implications. It is axiomatic that an immunological reaction will occur where the antigen is localized.

Address requests for reprints to Dr. Leighton E. Cluff, Department of Medicine, University of Florida School of Medicine, Gainesville, Florida 32603.

Therefore, if microorganisms localize in skin, bone or kidney any immunological reaction occurring in the infection will most likely occur where the bacteria are. For example, in encephalitic or meningitic virus infection, localization of virus in the central nervous system may result in an immunological reaction within the central nervous system if the microorganism or its antigen remain localized until the immunological response develops.

Antigen elaborated by microorganisms may localize differently than the whole microorganism and this may result in lesions unassociated with viable microbes. For example, a typical allergic type nephritis may occur in trichinosis, presumably attributable to an immunological reaction with parasitic antigen, yet the trichina never localize in the kidney. It must be presumed, therefore, that antigens of the trichina may localize in the kidney.

Chemical mediators of immunological reactions may produce widespread effects unassociated with widespread distribution of antigen, but it is often difficult to attribute morphological lesions to these chemical mediators.

It may be impossible to separate the effects of immunological reactions in infection from the injurious or toxic action of the microorganism itself. For example, perivascular lymphocytic cuffing in the central nervous system in encephalitis may develop at the time the immune reaction to the virus occurs, but also at a time when the virus titer in the central nervous system is high. It is difficult in such instances to be certain of the mechanism of production of the lesion. New evidence and techniques have assisted in differentiating these effects but more needs to be done. Of course, one does not find this difficulty when studying immunologic reactions to noninjurious, nontoxic antigens, but immune reactions probably produce lesions in infection as readily as they do following inoculation of noninfectious antigen.

Bacteria of the same species may have common as well as differing antigens, and infection may occur repetitively with various strains of these bacteria. Illustrative of the probable immunological consequences of infections by bacteria of the same species with varying but common antigens is the occurrence of rheumatic fever following infection by Group A Streptococci. Group A Streptococcal types have different cell wall protein but other antigens in common. The possible implications of immunological reactions to common antigens of different bacteria of the same species have been little explored, but are probably significant.

Persistence of the immunological response following infection has been attributed to persistence of antigens or microorganisms in the tissues. Whether or not persistence of antigens is always necessary for persistence of the immunological response is not known. There are some infections, however, in which the microorganism may persist in the tissues for very long periods of time. Persistence is known in tuberculosis, brucellosis, staphylococcal osteomyelitis, typhoid fever, parasitic disease and herpes simplex. In many of these instances persistence of the antigen or microbe may maintain the immunological response, but persistence of nonreplicating microorganisms is not responsible for progressive infection. Only when the microorganism begins to replicate does infectious disease occur. In the absence of rapid replication, however, we have the most readily available evidence that immunological reactions may be responsible for some of the manifestations of disease.

Occasionally, recovery from infection does not result in sufficient acquired resistance to prevent recurrent infection by the same organism. This is exemplified by staphylococcal disease, tuberculosis, salmonellosis, shigellosis and influenza. In these situations, immunological reactivity with the organism may not prevent infection but could play a significant role in producing manifestations of illness upon reinfection.

A peculiarity of bacteria is that they can be selectively affected by antimicrobial drugs, causing cessation of growth or lysis of the microorganism. This action of antibiotics has interesting effects upon the immunological response not seen with nonviable antigens. For example, administration of an antibiotic early in the course of infection may reduce the antigenic mass, interfering with the induction of an immunological response. Such suppression of the immunological response may interfere with the development of acquired resistance, but also may interrupt adverse immunological reactions precipitated by antigens of the microbe. This may be the mechanism of prevention of rheumatic fever by prompt treatment of streptococcal infection. In addition, administration of an antibiotic during the course of infection, after the immunological response has developed, can liberate bacterial antigen by lysis of the microorganism leading to systemic reactions as characterized by the Herxheimer reaction.

From these remarks it should be clear that the

immunological response of the animal to antigens of microorganisms may be little if at all different from the immunological response to other antigens, but the unique characteristics of viable pathogenic microorganisms can significantly influence the role of immunological reactions in causing manifestations of illness.

Chronic infection in which the microorganism persists and replicates beyond the time of emergence of the immunological response would most likely be associated with manifestations attributable to hypersensitivity. This explains the considerable work on the role of hypersensitivity in tuberculosis. In addition, however, recurrent infection attributable to microorganisms which induce little if any acquired resistance to reinfection, might be expected to result in manifestations of illness associated with hypersensitivity reactions. Indeed, clinical and expermental studies have shown that recurrent staphylococcal disease is characterized by increased cellulitis about the site of infection and increased susceptibility to infection associated with development of bacterial hypersensitivity.

Immunological mechanisms have been incriminated in production of manifestations of illness in infections with long incubation periods. In tuberculosis, for example, many of the manifestations of disease arise with the appearance of tuberculin allergy about six weeks after initation of infection. Similar observations in brucellosis also have suggested that immunological mechanisms serve to produce manifestations of illness.

Many events influence the incubation period of infection other than the delay in emergence of the immunological response. These include the dose of microorganism, degree of nonspecific or specific resistance to infection and route of invasion by the microorganism. Nevertheless, infections producing disease only after a lag period commensurate with the appearance of the immunological response should be suspected as possible examples of hypersensitivity producing disease.

The manifestations of most acute self limited infections may not be precipitated by an immunological reaction. Rheumatic fever and glomerulonephritis, however, may be examples of reactions resulting from acute infection not associated with persistence of infection. It is possible, therefore, that microorganisms may initiate immunological reactions causing disease after subsidence of the infection itself. Whether or not this phenomenon is attributable to an immunological reaction with persistent microbial antigen separate from the viable microorganism or to an immunological reaction of another sort remains to be shown. Recent observations, however, suggest that certain microbial antigens may be immunologically related to host antigens and immunological reactions to the microorganisms might be responsible for a form of autoimmunological disease. In addition, studies of polyoma virus and Rous sarcoma virus infection suggest that some microorganisms can cause appearance of new cell antigens associated with emergence of neoplasia and this new cell antigen may induce an immunological response capable of reacting against the host's own tissues and produce a homograft type reaction. From these observations, therefore, we cannot dismiss acute self limited infections as possible mediators of untoward immunological reactions producing manifestations of illness.

Almost any infection may, in one way or another, initiate immunological responses capable of causing cell and tissue injury. The full importance of microorganisms in initiating obscure immunological reactions, however, remains to be determined.

Fever during some infections, particularly tuberculosis, has been related to immunological reactions with microbial antigens.

Urticaria has been attributed to infections including pyelonephritis and dental abscesses. It is of interest, however, how rarely one sees urticaria in infection except in parasitic infestation such as echinococcosis, trichinosis and schistosomiasis. The explanation for urticaria in parasitic infection is obscure. However, antigens of parasites have a unique propensity for induction of reagen-like hypersensitivity. The peculiar localization of parasites, their confinement to the intestinal tract, or encystment within muscle or viscera, and perhaps other features could profitably be explored to explain the urticarial reaction and eosinophilia commonly seen in these diseases.

The rash of typhus has been related to an immunological reaction with rickettsia. Erythema nodosum is commonly observed in coccidioidomycosis and occasionally in streptococcal and tuberculous infection. Histopathologically, erythema nodosum resembles the perivasculitis or arteritic lesions of experimental serum sickness and periarteritis nodosa. That erythema nodosum is due to hypersensitivity is reasonably well established in infection as these lesions can be induced in the sensitized person with antigens derived from the responsible microorganism. Why erythema nodosum is localized

to extensor surfaces of the extremities is obscure. Perhaps microbial antigen localization leads to production of the lesion. Such localization is seen in rickettsial infection, as the organism can be identified in the vasculitis and petechia.

Horses injected with pneumococci for production of antiserum often developed endocarditis following inoculation of the virulent microbe into immune animals. It has also been demonstrated that inoculation of other microorganisms intravenously into partially immunized animals can induce bacterial endocarditis. Inoculation of these bacteria into non-immunized normal animals will not produce endocarditis. Whether or not partial immunity is instrumental in developments of bacterial endocarditis in man is not known, but in most instances serum antibody to the infecting microorganism usually is found in the blood during the course of the infection and bacteremia. Indeed, in pneumococcal endocarditis in man the presence of capsular antibody can often be found in the serum and the pneumococci may show a quellung reaction or capsular swelling on direct examination of the blood. Normal guinea pigs inoculated with amoebae directly into the portal vein produce transient inflammatory foci in the liver which resolve without development of abscesses. Similar inoculation of amoebae into animals with chronic intestinal infection or into animals immunized with antigens of the amoebae results in development of large chronic abscesses in the liver. It seems probable, therefore, that immunological reactions to microorganisms may be of similar importance in localization of other types of infection, but this has not been extensively explored.

Glomerulonephritis usually is considered a possible immunological consequence of Group A streptococcal infection, and resembles the nephritis induced by experimental immunological procedures. It is not as well appreciated that nephritis morphologically indistingushable from poststreptococcal glomerulonephritis occurs in subacute bacterial endocarditis and trichinosis. The most uniform presence of high titered serum antibody in the blood against the microorganism causing endocarditis and bacteremia suggests the possibility that the nephritis of this disease may be attributable to an immunological reaction. Simularly, the invariable presence of hypersensitivity to antigens of trichina at the onset of manifestations of trichinosis, and the frequent occurrence of urticaria, vasculitis and eosinophilia in this disease, suggest an immunological pathogenesis of the manifestations of the illness. In addition, hemorrhagic glomerulonephritis and encephalitis are occasionally seen in trichinosis in the absence of localization of the parasite in brain or kidney.

Postvaccinal and postinfectious meningoencephalitis have been attributed to immunologic reactions with virus localized in the central nervous system, or with brain tissue itself. That this process represents an autoimmune disease seems unlikely. That the illness represents an immunological reaction is in dispute, but there is convincing evidence that some forms of viral meningoencephalitis are immunologically determined. Administration of virus specific antiserum to mice 24, 48 and 72 hours after injection of Venezuelan equine encephalomyelitis virus, for example, can precipitate pathological lesions in the brain even though virus titers in the animals are thereby reduced.

Hemolysis may occur during or following infection and can be attributed to induction of hemolysin by direct involvement of the erythrocyte as in bartonellosis, or by another immunological process. These immune hemolytic anemias of infection usually occur during convalescense from the infection as in primary atypical or mycoplasma pneumonia.

In the immune hemolysis following viral or bacterial infection hemaglutinins or cold hemolysins may be found in the serum. In most instances these hemolytic antibodies act upon normal erythrocytes as well as upon erythrocytes from the affected person. The mechanism of induction of this immunological response is not clear, but it has been reported that influenza virus acting upon human erythrocytes can induce changes in the antigenicity of the red cells. This effect of a virus upon erythrocytes inducing altered antigenicity may explain one mechanism whereby infection can induce an immunological response to the host cells. The cold agglutinins or hemolysin appearing in the serum of patients two to three weeks after primary atypical or mycoplasma pneumonia may give a positive direct Coombs test and are probably responsible not only for anemia but can also be associated with Raynaud's phenomena and hemoglobinuria.

Sterile arthritis or arthralgia is a common manifestation of infection and of many hypersensitivity reactions. We (Charache, P. and Lewis, G.) have shown that intravenous injection of pneumococci or staphylococci into rabbits can result in production of arthritis occasionally delayed in onset 7 to 11 days and associated with appearance of an immunological response to the bacteria. The arthritis in these animals is not associated with the presence of viable bacteria in the joint. It is our interpre-

tation that the microorganism or its antigen may become localized in the synovia and an immunological reaction to the organism is responsible for the arthritis. The arthritis produced in joints of rats by subcutaneous or intradermal inoculation of a mycobacterial adjuvant, perhaps, is due to a similar mechanism. The phagocytic function of synovial cells and the peculiar localization of allergic reactions in joints may explain the frequency of arthritis in infection.

There are many other interesting and important manifestations of infection which may be attributable to immunological reactions. Nonspecific immunological responses are also a consequence of infection, including development of Wassermann antibody, rheumatoid factor and amyloidosis. The Wassermann antibody is directed against cardiolipin, an antigen derived from human, bovine and other animal cardiac tissue. In this sense, it is an auto-antibody appearing in patients with syphilis. A nonpathogenic Treponema has been shown to possess a lipid antigen cross-reacting with antibody to cardiolipin, but the occurrence of Wassermann antibody during infection not attributable to Treponema; such as in infectious mononucleosis, leprosy, leishmaniasis and other acute and chronic infections, suggests that cardiolipin antibody may be due to autosensitization initiated by infection. It has been shown that cardiac antigen inoculated into the same animal species does not induce production of antibody unless the antigen is injected along with a foreign protein or adjuvant. On the basis of this evidence it is postulated that infection by Treponema pallidum or other microorganisms acts as a carrier rendering the autologous cardiolipin antigenic and inducing Wassermann or cardiolipin antibody. It is still possible that many of the late, chronic manifestations of syphilis are attributable to this phenomenon.

Rheumatoid factor appears in the serum of human beings and experimental animals during active tuberculosis, syphilis, Group A streptococcal infection and subacute bacterial endocarditis. In animals it has been induced by inoculation of coliform and typhoid bacilli. We have recently observed the appearance of rheumatoid factor in the serum of 28 percent of patients intensively vaccinated with a variety of bacterial, viral and rickettsial antigens. The implications of rheumatoid factor in the pathogenesis of the manifestations of illness, however, are as obscure in infection as in rheumatoid arthritis. Structural alteration of immunoglobulin as a result of antigen-antibody reactions may stimulate production of antiglobulin antibody and may explain the development of rheumatoid factor following vaccination or during infection, related to a reaction between antibody and the microorganism. Rheumatoid factor may aggravate arthritis and it has been suggested that rheumatoid factor may produce vasculitis. Nevertheless, transfer of blood containing high titers of rheumatoid factor into normal persons fails to produce deleterious effects.

Amyloidosis has been produced in almost every animal species by hyperimmunization with many bacterial and nonbacterial substances. The pathogenesis of amyloid deposition in chronic suppurative infection implicates an immunological disorder.

This discussion of the immunological disorders of infection attempts to define those properties of microorganisms which influence immunological responses and reactions differently than the immunologic reactions to nonviable, noninfectious antigens. In addition, I have indicated the types of infection in which immunologic reactions might be expected to produce manifestations of illness. Very few infections can be excluded as unassociated with immunological reactions that can produce untoward effects, and there are many manifestations of infectious illness that have been attributed to immunologic reactions. Many of these are poorly substantiated. I have illustrated the variety and peculiarities of the effects of immunologic reactions in the infectious process, without attempting to discuss the many features thought to be due to hypersensitivity. I have not discussed another important aspect of hypersensitivity in infection; allergic reactions to antimicrobial drugs.

Interest in immunology arose from consideration of infectious disease, but the focus of attention has been primarily towards immune mechanisms as involved in acquired resistance and less attention has been given to the implications of immunologic reactions in producing manifestations of illness in infection. Despite this, there is little to indicate that immunologic disease arises any less frequently from reaction to microbial antigens than from reactions to other antigens. The ubiquitousness of microorganisms in our environment and the frequency of infection by benign and malignant microorganisms suggests that infection may be one of the more important causes of immunologic disorders in man.

(The references may be seen in the original article.)

ACUTE EPIGLOTTITIS: CHALLENGE OF A RARELY RECOGNIZED EMERGENCY

J. D. Andrew, MB CH B MRCP ED DCH, O. P. Tandon,† MB BS DCH, and D. C. Turk,‡ DM MRCP MC PATH, Brit Med J 3(5617):524–526, August 31, 1968.*

Summary: Acute epiglottitis is a fulminating infection of young children, requiring urgent and specific treatment. Most cases are caused by infection with Haemophilus influenzae type b. Only a few cases, nearly all of them fatal, have been reported from Britain, but probably many others go unrecognized. Of four cases seen by us in the past six years three survived, having responded rapidly and completely to treatment. This consisted chiefly of measures to deal with respiratory tract obstruction and parenteral administration of antibiotics. There is need for a widespread awareness of the existence, presenting features, and extreme urgency for treatment of this disease.

Introduction

"Acute epiglottitis is a serious and often fatal condition that, although infrequently recognized, lends itself to accurate bedside diagnosis with consequent institution of specific life-saving therapy. Its recognition and management should become familiar to all concerned with the care of sick children" (Berenberg and Kevy, 1958). This condition was clearly defined and distinguished from laryngotracheitis, diphtheritic or presumptively virus croup, and other acute respiratory tract infections by Sinclair (1941), Alexander, Ellis, and Leidy (1942), De Bois and Aldrich (1943), Miller (1948), and Rabe (1948) on the basis of their experience in different parts of the U.S.A.; but even in that country as recently as 1958 Berenberg and Kevy had to report that only one of their 42 cases was correctly diagnosed before reaching hospital. The condition occurs mainly in children age 2 to 7 years, but sometimes also in infants, older children, or even adults.

Characteristically, a previously healthy child develops a sore throat and increasing dyspnoea, and then within a few hours of onset becomes so severely ill that the terms "shock," "prostration," and "collapse" have been used by different authors to describe the general condition. Examination of the respiratory tract shows pharyngitis and laryngitis with supraglottic oedema, but the pathognomonic feature, which may be missed unless the tongue is depressed or pulled forward, is a swollen red epiglottis that "bears a striking resemblance to a bright red cherry obstructing the pharynx at the base of the tongue" (Berenberg and Kevy, 1958). Urgent tracheostomy or other measures to maintain an airway are usually necessary, and the infection requires prompt and adequate treatment. Chloramphenicol or ampicillin should be used for this, since it is generally accepted that the condition is due to capsulated type b strains of *Haemophilus influenzae*. Even Berenberg and Kevy (1958) and Vetto (1960), who suggested on rather inadequate bacteriological evidence that other bacteria are responsible for some cases, agreed that type b *H. influenzae* is the commonest cause.

The reports mentioned so far all came from the U.S.A. The British literature on this disease is scanty, but there are good reasons for believing that this is a result of its infrequent recognition rather than of its rarity. The boy reported by De Navasquez (1942) as having died in London of "acute laryngitis and septacaemia due to *H. influenzae* type b" was presumably a victim of the condition that we are discussing, though the state of his epiglottis was not mentioned in the report.

No further relevant British papers appeared until Camps and Jones (Camps, 1953; Jones and Camps, 1957; Jones, 1958) described a total of 33 cases of epiglottitis seen by them in a period of 14 years. *H. influenzae* type b was incriminated in all cases in which adequate bacteriological investigation was carried out. Four patients were successfully treated, but the other 29, including the only adult, died. Jones and Camps (1957) described the fact that 26 of their first 29 cases had come to coroners' post-mortem examinations as "a challenge to the general practitioner, the paediatrician, and the laryngologist"; and a further challenge is provided by the fact that these two men who became interested in this condition were able to recognize so many cases in the course of their routine work. But these challenges have not been taken up. A few more deaths from epiglottitis have been reported in this country recently (Johnstone and Lawy, 1967; Gardner, Turk, Aherne, Bird, Holdaway, and Court, 1967; Crome, Erdohazi,

* Children's Department, Bishop Auckland General Hospital, Co. Durham.
† Children's Department, Royal Victoria Infirmary, Newcastle upon Tyne.
‡ Microbiology Department, Medical School and Royal Victoria Infirmary, Newcastle upon Tyne.
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and Lawson, 1968), but no more survivors. The experience of Camps and Jones strongly suggests that this disease may well be responsible for a substantial number of unexplained but avoidable deaths of children in Britain.

W have seen four cases of epiglottitis in the past six years, and have been able to confirm the *H. influenzae* type b was responsible for at least two of them. One of these has already been reported (Gardner *et al.,* 1967). The patient, a 21-month-old boy, was moribund before he reached hospital, and the diagnosis of epiglottitis was made only at necropsy. Case summaries for the other three patients are given below. In each case the diagnosis of epiglottitis was made soon after the child reached hospital, and all three responded well to treatment. In no case was there a history of relevant preceding illness affecting the patient or any member of the family.

Case 1

A 5-year-old-girl, the older of two daughters of a coal miner, was admitted to the Royal Victoria Infirmary in November 1962. Nine hours earlier she had complained of a sore throat. Later she became drowsy, vomited a little mucoid material, became blue in the face, and was taken to her family doctor's house and then immediately to the hospital. On admission she was dyspnoeic, with pharyngeal gurgling and respiratory stridor. Her epiglottis was seen to be swollen and red, but the pathognomonic significance of this was not realized at first. She was placed in a humid atmosphere and her throat was sprayed with hydrocortisone. After half an hour the nature of her illness was recognized. At this stage respiratory obstruction suddenly became complete. It was temporarily relieved by insertion of an endotracheal tube. Tracheostomy was performed three-quarters of an hour later. She received intravenous tetracycline and sedatives and was maintained in a humid atmosphere in an oxygen tent, with rapid improvement. The tracheostomy tube was removed after 60 hours. She went home in good health one week after admission.

Her blood picture on admission showed a moderate anaemia and 21,000 polymorphs per cu. mm. No apparently relevant bacteria were isolated from throat and cough swabs. Blood culture was not carried out. Antibody determinations by the method of Turk and Green (1964) showed a rise of antibody titre for *H. influenzae* type b capsular antigen from less than 4 in a serum sample collected from the patient on admission to 256 in one collected seven weeks later, with no change in the titres for the other five types of capsulated *H. influenzae*.

Case 2

Another 5-year-old girl, the youngest of three children of a sales-manager, was admitted to Bishop Auckland General Hospital in November 1967. She had complained of shivering and soreness of the mouth and throat 11 hours earlier, and during the next seven hours had become breathless, restless, and distressed. She was referred to the hospital with a diagnosis of laryngotracheitis. Two hours after admission she was noted to have oedema of the neck and a markedly swollen red epiglottis, and the diagnosis of epiglottitis was made. As in the previous case, respiratory obstruction suddenly became complete at this stage. It was relieved by using a laryngoscope to displace the epiglottis forwards, and marked oedema of the larynx could then be seen. Attempts at intubation were unsuccessful, and it was necessary to keep the laryngoscope in place for about two hours. Meanwhile the child was in an oxygen tent with a high humidity level, and received intramuscular streptomycin and chloramphenicol, hydrocortisone, and sedatives. Tracheostomy was considered at first but was made unnecessary by her rapid response to these other measures. Thirty hours after admission she was sitting up and talking but was still hoarse, with some reddening and swelling of the pharynz and epiglottis, and so she was kept in the humid oxygen tent for a further day. She went home in good health nine days after admission.

Her blood picture on admission showed 25,000 polymorphs per cu. mm. A chest radiograph showed some left lower lobe consolidation. Nose and throat swabs were collected on admission but were then mislaid, and there was an excessive delay before they reached the laboratory; no relevant bacteria were grown. Blood culture was not carried out. Blood samples for antibody determinations were collected from the patient and both parents four months after her illness; no abnormal levels of antibodies for any of the capsulated *H. influenzae* types were found.

Case 3

A 3-year-old boy, the elder of two sons of a research scientist, was admitted to the Royal Victoria Infirmary in February 1968. Apart from nasal discharge for a few days he had been well until nine hours before admission, when he was noticed to be feverish and restless. Four hours later he was having

difficulty in clearing white mucus from his throat and mouth, and after a further two hours he suddenly became dyspnoeic, with stridor. His family doctor was called, diagnosed croup, and immediately arranged his admission to hospital. On admission he was a seriously ill child and was noted to have large congested tonsils, large tender tonsillar lymph nodes, a swollen red epiglottis, inspiratory stridor, and suprasternal and intercostal recession on inspiration. Epiglottitis was diagnosed. He was placed in a humid oxygen tent and was given ampicillin intramuscularly at once and for the first three days and orally for a further three days. For two hours after his admission it appeared possible that he would need tracheostomy, but from that time he improved rapidly. He was kept in the humid tent for six days, as his epiglottis was still enlarged and red and his voice was hoarse. He went home in good health nine days after admission, but his epiglottis was still enlarged 10 days later.

His blood picture on admission showed 21,000 polymorphs per cu. mm. *H. influenzae* type b was grown from nose and throat swabs and from blood culture on admission, from swabs of the epiglottis throughout his time in hospital and 10 days after his discharge, and from nose and throat swabs three months later. Nose and throat swabs were collected from his parents and brother two days after his admission and also three months later, but no capsulated haemophili were isolated. Blood collected from the mother two days after his admission had a somewhat raised titre of antibodies for *H. influenzae* type b (32; we regard 16 as the upper limit of normal), but no such antibodies were detected in blood collected from the father at the same time. No blood samples were collected from the two boys.

Virological Investigations

The virological investigations are included by courtesy of Dr. P. S. Gardner. Admission throat swabs and acute and convalescent serum samples from Cases 1 and 3 were examined by the techniques described by Andrew and Gardner (1963) for evidence of virus infection. No such evidence was found. In particular, there was no evidence of infection with respiratory syncytial virus, the other potential pathogen, besides *H. influenzae* type b, which was isolated in the fatal case mentioned above (Gardner *et al.*, 1967).

Discussion

It seems certain that without appropriate treatment each of these three children would have died within 13 hours or less of the first signs of illness, and in each case several of those hours had passed before it became clear that the illness was serious. They survived because their parents were observant and quick to seek help, because their family doctors wasted no time in arranging admission to hospital, and because their illness was recognized and appropriate measures were taken soon after they reached hospital. It is all too easy to see how less fortunate children with this disease could die from unidentified acute respiratory infections; and it is literally of vital importance that family doctors and paediatricians should be aware of the existence, features, and treatment of epiglottitis.

Aetiology

Upper respiratory tract swabs have serious limitations as sources of information for the diagnosis of epiglottitis. Isolation of *H. influenzae* from such specimens is meaningful only if the strain isolated is of type b, since non-capsulated strains are commonly present and may be numerous in the upper respiratory tracts of healthy people, and capsulated strains of types other than b have not been known to cause epiglottitis (Turk and May, 1967; Turk, 1967). On the other hand, Sinclair (1941), Alexander *et al.* (1942), and others have found that swabs of the nose, of the throat, and even of the surface of the epiglottis itself may fail to yield *H. influenzae* type b in cases in which it is present in the blood—and inside the epiglottis (Jones and Camps, 1957)—and is the undoubted cause of the epiglottitis.

Blood culture before the patient has received any antibiotics is thus the most useful bacteriological investigation. It was carried out in one of our patients (Case 3), with conclusive results, but it happened that in this case the causative role of *H. influenzae* type b was already clear from swab cultures. The serological findings in Case 1 indicate that the same organism was responsible. We have no evidence of the cause in Case 2. The absence of a raised level of antibodies for *H. influenzae* type b in the child's blood four months after her illness does not rule out this organism as the cause. There are other ways of explaining this finding, one of them being that the combination of streptomycin and chloramphenicol eradicated the infecting organism before it had been present long enough to cause an antibody rise.

Incidence

Like haemophilus meningitis, which is the commonest disease caused by *H. influenzae* type b, epi-

glottitis occurs sporadically and case-to-case spread is rarely demonstrated, though not unknown (Good, Fousek, Grossman, and Boisvert, 1943). But haemophilus meningitis commonly affects the youngest child in a family, and many of its victims are under 1 year old, whereas epiglottitis tends to occur in somewhat older children, as indicated in our small series. However, both conditions may be present in the same child, as in two of Jones and Camps's patients and in a 2-year-old girl who died in Carlisle in December 1967 (personal communication, Dr. F. M. Elderkin). Nasopharyngeal carriage of *H. influenzae* type b or seriological evidence of recent carriage are common findings in the families of children with haemophilus meningitis (Good *et al.,* 1943; Turk, 1963 and unpublished findings; Turk and May, 1967), but our limited studies of the families of two of our patients give no clear indication of a similar situation in relation to epiglottitis.

Treatment

Alexander *et al.* (1942) advised tracheotomy before a child with epiglottitis becomes desperately ill, rather than waiting in the hope that this is one of the mild cases that will not need it. However, with modern antibiotic treatment the period of serious illness can be very short, as shown by our patients, and recovery can be almost as dramatically rapid as onset of the disease. A humid atmosphere and temporary mechanical means of keeping a clear airway may be sufficient to carry the patient through the critical period. It has been suggested that laryngoscopy may introduce additional hazards (Jones and Camps, 1957).

Antibiotic treatment of haemophilus infections has been reviewed by Turk and May (1967). The failure of ampicillin to eradicate the haemophilus from the upper respiratory tract of our third patient may well have been due to failure of the antibiotic to penetrate the mucosa once inflammation has subsided, just as it fails to reach the sputum once bronchial inflammation subsides (May and Delves, 1965). The failure of this drug to eradicate an apparently sensitive strain of *H. influenzae* type b from the cerebrospinal fluid of a child with meningitis has recently been reported (Greene, 1968).

We are grateful to Dr. F. J. W. Miller for allowing us to publish details of a patient under his care (Case 1), and to Professor S. D. M. Court for encouraging us to write this report and for his helpful advice.

(The references may be seen in the original article.)

GENETIC ASPECTS OF GASTROINTESTINAL DISEASE

Kenneth L. Becker, MD, PhD, Med Clin N Amer 52(6):1273–1283, November 1968.*

As a result of the recent growth of interest in human genetic disease, many heritable conditions have been revealed in which the gastrointestinal tract is affected. Similarly, clinical and laboratory studies of the various gastrointestinal diseases have clarified or revealed heretofore vague or unsuspected genetic influences.

The gene has a broad mission: it must perpetuate itself within the body, and be propagated beyond the confines of that body to insure the continuance of the species. In addition, the gene has the ultimate and primary responsibility for inducing somatic structure and organization during development, and for maintaining biochemical function in adulthood. It is the sequence of bases in the DNA molecule which determines the identity and nature of a gene. The principal action of many genes is to specify the amino acid content and sequence of polypeptides. Indeed, it appears that the motive force in protoplasm is the translation of DNA sequences into specific polypeptide sequences, which may be enzymes or structural proteins. Hence, via the intermediary of protein synthesis, it is the genes which ultimately determine ontogeny and lead to the development in the individual of the physiological and morphological aspects of the phenotype.

Genetically determined gastrointestinal disease may be manifested by altered *function* or altered *structure*. For discussion, the term "altered function" will be used to denote abnormal physiological or pathological action. This dysfunction may or may

* Chief, Section of Metabolism and Genetics, Veterans Administration Hospital; Assistant Professor of Medicine, George Washington University, Washington, D. C.

not be dependent upon aberrations in enzymatic biochemical processes. The term "altered structure" will be used to denote genetically determined morphological anomalies in which there is no readily apparent enzyme abnormality.

For the purposes of this discussion, the genetic aspects of gastrointestinal disease have been subdivided into five arbitrary categories:

1. Single-gene gastrointestinal disease of altered structure.
2. Single-gene gastrointestinal disease of altered function.
3. Primary gastrointestinal disease with extragastrointestinal symptomatology.
4. Nongastrointestinal disease with occasional associated gastrointestinal symptomatology.
5. Polygenic influences on gastrointestinal disease.

Single-Gene Gastrointestinal Disease of Altered Structure

The phenogenesis of structural traits is particularly complex because it involves not only the synthesis of protein, but also cellular organization and differentiation. Clinically, those diseases of altered structure in which the heritable influences appear to be most apparent are single-gene diseases. An excellent example of single-gene gastrointestinal disease of altered structure is the Peutz-Jeghers syndrome. In 1921 Peutz described a family with polypoid lesions of the bowel and skin hyperpigmentation. After several other reports of similar cases had appeared in the literature, Jeghers and coworkers reported 10 additional patients and described the clinical and genetic aspects of the syndrome. In addition to polyposis, these patients manifest melanin pigmentation of the lips, the oral mucosa, and occasionally the fingers. The polyps involve primarily the small intestine, but may occur elsewhere in the gastrointestinal tract; they are rarely, if ever, premalignant. This syndrome is an excellent example of *pleiotropism*—that is, multiple effects of a single gene.

The pattern of transmission within the pedigree of the Peutz-Jeghers syndrome is typical of mendelian dominant inheritance: transmission of the trait is vertical from one generation to the next. Theoretically, 50 percent of the children of one unaffected parent and one heterozygously affected parent will have the trait; the normal relatives of an affected person will have normal children. In actuality, the inheritance of Peutz-Jeghers syndrome is less clear-cut because of variability in penetrance and expressivity, and perhaps because of mutations.

Familial polyposis of the colon, another example of a single-gene gastrointestinal polyposis, is somewhat more common than the Peutz-Jeghers syndrome. This disease, which also exhibits dominant transmission, may vary in severity from several isolated adenomas to involvement of the entire colon and rectum with multiple polyps. In contrast to the Peutz-Jeghers syndrome, there is no associated mucocutaneous pigmentation. The polypoid lesions frequently give rise to colonic carcinoma which may occur at an early age, is often multicentric, and grows rapidly. A distinct variety of intestinal polyposis, termed Gardner's syndrome, also transmitted dominantly, is associated with epidermoid cysts, fibromas of the soft tissues, and osteomas of the skull. The polyps may occasionally involve the small intestine and are premalignant.

Genetic disease of altered gastrointestinal structure can be clinically evident at birth. Thus, anorectal anomalies (imperforate anus or rectal fistula) with apparently dominant transmission have been noted in several families. Weinstein reported three families with imperforate anus in which X-linked recessive inheritance seemed likely, while the cases of Van Gelder and Kloepfer suggested autosomal recessive inheritance. The lack of uniformity in the transmission of these defects suggests a heterogeneity of genetic causes (nonallelism). It should be noted, however, that most cases of imperforate anus appear to be isolated occurrences, and only rarely are there any heritable influences discernible.

Other examples of single-gene structural diseases include familial extrahepatic biliary atresia of seemingly recessive inheritance, a pedigree of apparently autosomal dominant bilateral inguinal herniae which involved males of four generations, and situs inversus viscerum of suspected autosomal recessive transmission.

Single-Gene Gastrointestinal Disease of Altered Function

As the elegance of biochemical, analytical, and diagnostic techniques increases, so does the list of known genetically induced diseases of altered gastrointestinal function. Occasionally, it appears that a biochemical or enzymatic defect causes the dysfunction, although more frequently no specific metabolic error has been elucidated. Since many of these illnesses have been described only recently, knowledge concerning the mode of inheritance is often rudimentary. Thus, the description of a disease in two or more members of several sibships without apparent parental morbidity suggests recessive trans-

mission, as does the description of one or more involved children born of uninvolved parents who are consanguineous. For example, recessivity has been postulated by Sheldon in his report of two unrelated sibships with congenital absence of pancreatic lipase. The parents were normal. The illness was characterized by oily, floating, bulky stools, with normal somatic growth and without associated abdominal distention, anemia, or abnormal sweat electrolyte concentrations. Analysis of the duodenal aspirate demonstrated deficiency or absence of pancreatic lipase. The children responded to treatment with pancreatic extract. On the other hand, involvement of three successive generations with a bizarre myopathy characterized by the insidious onset in late life of slowly progressive dysphagia and symmetrical ptosis of the eyelids (oculopharyngeal muscular dystrophy) led Victor and co-workers to conclude that this disease was transmitted dominantly.

Gross and co-workers have demonstrated that even a variety of pancreatitis may be determined by a single-gene defect. These patients are characterized by a clinical history similar to that of chronic relapsing pancreatitis except for early age of onset, equal sex incidence, stones in the larger pancreatic ducts, and infrequency of accompanying alcoholism or gallstones. Some of these patients excrete abnormal amounts of cystine and lysine in the urine. The disease appears to be transmitted as a dominant trait.

The highly inbred old order Amish have been a fertile source for genetic studies. Byler's disease, or fatal familial intrahepatic cholestasis, has been found in these isolates. Children with this disease manifest early onset of loose foul-smelling stools, recurrent jaundice, hepatosplenomegaly, dwarfism, elevated serum alkaline phosphatase, and normal to low serum cholesterol. Transmission appears to follow an autosomal recessive pattern. Another form of genetic nonhemolytic jaundice is the Crigler-Najjar syndrome. This severe, persistent neonatal disease is characterized by a defect of glucuronic acid conjugation of bilirubin (glucuronyl transferase deficiency). The sibship aggregation found in this disease strongly suggests that these patients are homozygous for a mutant gene, the illness therefore being transmitted recessively.

Another inborn error of bilirubin metabolism is the Dubin-Johnson syndrome, genetic defect of bilirubin excretion transmitted as an autosomal dominant with much variability of expression. Clinically, there is hyperbilirubinemia of the conjugated type, increased retention of bromsulphalein dye, frequent nonvisualization of the gallbladder, and abnormal pigmentation of the liver parenchyma.

There appear to be several single-gene defects of intestinal absorption. Among these, the heritable deficiencies of sugar-splitting enzymes are arousing considerable attention. Congenital juvenile sucrase and isomaltase deficiency is characterized by diarrhea induced by sucrose or isomaltose ingestion, which is ameliorated by dietary exclusion of these sugars. The mode of transmission of this disease is uncertain. An analogous disease, primary monosaccharide malabsorption, apparently is due to a defect in the active transport of glucose galactose across the mucous membrane of the intestine. Fructose absorption is normal, as is disaccharidase activity. Histologically, the intestinal mucosa appears normal. This disease, which manifests as severe diarrhea in infants after commencement of breast feeding, may be transmitted recessively.

Another recently described genetic disease of intestinal malabsorption is familial protein intolerance with deficient transport of basic amino acids. The children manifest an aversion to protein-rich foods, episodes of diarrhea and vomiting, dwarfism, hyperammonemia, deficient rise in plasma urea levels following protein intake, aminoaciduria, and hepatomegaly which may eventuate in diffuse cirrhosis. The mode of inheritance appears to be recessive.

Evidence that the entire spectrum of manifestations and physical findings known as hemochromatosis is a genetic disease of abnormal intestinal absorption of iron is as yet insufficient and controversial. The criteria for diagnosis are disputed and the etiologic relationship to alcoholism is unresolved. However, Powell's study of iron storage in relatives of patients with hemochromatosis and in relatives of patients with alcoholic cirrhosis and hemosiderosis supported the belief that the two diseases are distinct entities, and that idiopathic hemochromatosis is genetically determined. A clinical and pedigree study by Debré and co-workers led to the conclusion that the idiopathic hemochromatosis patient may be heterozygous, and that some cases of juvenile hemochromatosis may be homozygous. Studies by other investigators have also emphasized the heritable aspects of this disease, but the mechanism of transmission is, as yet, uncertain.

Primary Gastrointestinal Disease With Extragastrointestinal Symptomatology

There are several genetic diseases in which some or all of the causative factors may reside in the gastrointestinal tract, yet severe extragastrointestinal symptons may occur, or may even dominate the

clinical picture. One example of such a disease is congenital beta-lipoprotein deficiency. These patients have steatorrhea, diffuse disease of the nervous system, occasional retinitis pigmentosa, and abnormal spiny-appearing erythrocytes (acanthocytes). Beta or low-density lipoproteins are absent or diminished, and it appears that these patients have a recessively transmitted inability to form the beta-lipoprotein molecule. The decrease in blood lipids appears to be due to the deficient lipoprotein transport, and the neurologic manifestations (neuropathy, ataxia) conceivably may be related to this primary defect.

Pernicious anemia is another disease in which some of the manifestations are extragastrointestinal, but in which the pathophysiologic abnormality apparently resides in the gastrointestinal tract. This abnormality is defective synthesis by gastric mucosa of the mucoprotein intrinsic factor necessary for intestinal transport of vitamin B_{12}. According to some investigators, adult pernicious anemia appears to follow an autosomal dominant inheritance pattern. Others have postulated that some forms of familial juvenile pernicious anemia might be due to homozygosity for a gene responsible for deficient secretion of intrinsic factor.

Nongastrointestinal Disease With Occasional Associated Gastrointestinal Symptomatology

Although principally entodermal in origin, the gastrointestinal system does not develop or function independently of other body systems. Thus, there are various genetic diseases which are not primarily diseases of the gastrointestinal tract but which occasionally result in gastrointestinal pathology or symptomatology. For example, Marfan's syndrome, a diffuse disease of connective tissue, has been associated with diaphragmatic hernia and with diverticulosis and diverticulitis of the colon. In such cases, it is not difficult to imagine that the same connective tissue defect which results in lax joints and dislocated lenses may also involve the gastrointestinal tract. Similarly, the genetic disease myotonia dystrophica (muscular wasting, lenticular opacities, frontal baldness, testicular atrophy) may involve the pharynx and esophagus.

Nongastrointestinal disease may causes abdominal pain. Acute intermittent porphyria is an inherited disease which is primarily due to abnormal pyrrole pigment metabolism, but which may cause severe episodes of abdominal pain simulating surgical emergencies. (Of course, since the liver may be the source of the porphyrin dyscrasia, one might justifiably prefer to call this a gastrointestinal disease.) Similarly, severe attacks of abdominal pain are found in association with diffuse angiokeratoma of Fabry. The pedigree data are consistent with X-linked recessive transmission of this disease—for example, predominance of involved males, no or minimal involvement by the carrier female, and no father-to-son transmission.

One of the earliest described human genetic diseases is hereditary hemorrhagic telangiectasia, a disease of dominant transmission characterized by multiple, sharply circumscribed, flat telangiectatic lesions of the face, lips, tongue, and mucosal surfaces of the respiratory, urinary, and gastrointestinal tracts. When the latter is involved, the patient is subject to hematemesis or melena. Gastrointestinal involvement in the dominant disease, neurofibromatosis, can also result in gastrointestinal bleeding, as can that genetically determined disease of elastic tissue, pseudoxanthoma elasticum. Blood in the stools is also seen in the X-linked Aldrich syndrome (eczema, thrombocytopenia, increased liability to infections).

Severe intractable peptic ulcer is recognized as being a gastrointestinal complication or concomitant feature of the dominantly transmitted syndrome of multiple endocrine adenomatosis (varying combinations of adenomas of the pituitary, parathyroids, pancreas, thyroid, and adrenal cortex). The extent of the relationship between this entity and the Zollinger-Ellison syndrome is, as yet, unclear.

Cirrhosis of the liver appears to be an occasional or frequent manifestation of several genetically determined diseases. The cirrhosis of the liver which is found in the recessively transmitted Wilson's disease (hepatolenticular degeneration) is common enough to be considered part of this syndrome, which is apparently due to an inborn error of copper metabolism. Galactosemia is an inborn error of metabolism in which there is a recessively inherited deficiency of galactose-1-phosphate uridyl transferase. It is associated with hepatic cirrhosis, as well as cataracts, feeding disturbances, and mental retardation. The biliary cirrhosis of the recessively transmitted disease mucoviscidosis (cystic fibrosis of the pancreas) is frequently only part of the total picture of pancreatic exocrine deficiency, sweat gland dysfunction, and chronic bronchopulmonary infection.

Progressive poliodystrophy with cirrhosis of the liver is a newly discovered disease which appears to be familial. It is characterized by convulsions, mental and growth retardation, atrophy of the cerebral gray matter, jaundice, and hepatic cirrhosis. Still another heritable disorder which may result in cirrhosis of the

liver is tyrosinosis. The recessively transmitted disease appears to be due to a congenital lack of p-hydroxyphenyl-pyruvate oxidase, leading to abnormal tyrosine metabolism with elevated serum tyrosine levels and increased excretion of this amino acid and its metabolites in the urine. This usually fatal disease of infants and children is characterized by vomiting and diarrhea, failure to thrive, abdominal distention, hepatic cirrhosis with hepatosplenomegaly, and renal tubular defects with vitamin D-resistant rickets.

Polygenic Influences on Gastrointestinal Disease

More commonly than not, gastrointestinal disease is determined or modified by multiple genetic factors which, as is the case with single-gene diseases, must interact with a myriad of environmental influences. Such a composite effect which is dependent on the interaction of several genes is termed *polygenic inheritance*. Because of the complexity of genic interactions, it is impossible to analyze this variety of inheritance by the classic pedigree methods.

A good example of polygenic influences acting upon gastrointestinal disease may be found in carcinoma of the stomach. There is no doubt that genetic factors are of importance in connection with some forms of cancer, the literature being replete with data suggesting that susceptibility to cancer may be inherited. Of course, susceptibility to disease does not necessarily mean morbidity. Whether cancer is due to latent viruses, carcinogenic substances, or somatic cell mutations, it is clear that in certain circumstances genetic factors can alter its incidence, progression, and manifestations. Perhaps because of its frequency, gastric cancer has been the subject of considerable genetic investigation. These various studies, though often not conclusive, have been particularly interesting.

It is known that the incidence of carcinoma of the stomach varies greatly in different regions of the world. Although the incidence appears to be decreasing in the United States, it is extremely high in Japan, where stomach cancer causes roughly 50 percent of all deaths from malignant diseases in males. There is a lower death rate from stomach cancer among Japanese immigrants in California than there is in Japan. Thus, since migrants from high-risk to low-risk areas have a lower incidence of stomach cancer, environmental factors do indeed seem important. For example, it has been suggested that the high incidence in Iceland is due to ingested polycyclic hydrocarbons found in smoked meat and fish. Undetermined environmental influences may also explain why stomach cancer is more common among poorer population groups in both Europe and North America.

However, there is some preliminary evidence of ethnic predisposition to carcinoma of the stomach which does not appear to be related to environmental factors. Several years ago, Legon called attention to a surprisingly high incidence of deaths due to stomach cancer in certain areas of Wales. In a recent epidemiological study, Ashley and Davies noted that the distribution of gastric cancer followed closely the distribution of Welsh surnames, even in areas where Welsh and non-Welsh lived side by side with apparently similar environmental, occupational, and culinary conditions.

In addition to ethnic factors, there appear to be some families with a disproportionately high incidence of cancer. Often, these pedigrees exhibit a heterogeneity of type and location of neoplasms. However, in some of these families it appears that there is a particular propensity toward gastric cancer. Certainly, the fact that carcinoma of the stomach occurs more often in any given pedigree than would be expected by chance suggests that there may be a genetic background influencing acquisition of the disease. However, broad conclusions concerning cancer-susceptible genotypes must be made with caution because of the tendency to report only those families with a high incidence of cancer. In addition, gastric carcinoma is not uncommon, and random distribution of this disease may result in several cases in one family. Nevertheless, the familial aggregation of gastric carcinoma is considerable, and the incidence of gastric cancer has been reported to be approximately four times higher among the relatives of patients with this illness than in a control population.

Studies of twins have suggested heritable factors in stomach cancer. Isolated case reports have described carcinoma of the stomach appearing in monozygous twins, although reported cases of nonconcordance are equally common. However, it does appear that there is a greater concordance for cancer of the stomach in monozygous twin pairs than in dizygous twin pairs. The result of the MZ-DZ comparison method suggest that, although there are heritable constitutional factors favorable to gastric cancer, environmental modifying influences are also important.

Another factor influencing the incidence of gastric carcinoma is the high incidence of the latter among pernicious anemia patients. The heritable aspects of this latter disease have been amply documented.

A final factor of importance in the consideration of the multifactorial genetic influences upon gastric can-

cer relates to the discovery by Aird and co-workers of the increased incidence of blood group A in patients with this disease. This relationship is true for areas of both high and low incidence, and has been confirmed by other investigators. How do the blood groups play a role in the susceptibility to, or the protection against, carcinoma of the stomach? Does the gene which determines the presence of blood group A have a pleiotropic effect, in that it may modify or enhance other genes which influence biochemical processes predisposing to carcinogenesis in the stomach? Does blood group A directly exert a toxic influence upon the stomach? The cellular ABO mucopolysaccharide antigens may occur in soluble form in saliva, and such persons are termed secretors. The ability to secrete these antigens is controlled by a secretor locus or loci. Initially, it was postulated that group A secretor substances may topically irritate the stomach and induce malignant change. However, it appears that the secretor is not unduly predisposed to carcinoma of the stomach. Other intriguing observations concerning blood group A which may have some relationship to gastric cancer are the apparent correlation of group A and gastric hypochlorhydria, and the association of group A and pernicious anemia.

Polygenic influences also have been implicated in ulcerative colitis and regional enteritis, and in duodenal ulcer. Undoubtedly, there are many other gastrointestinal diseases in which polygenic inheritance factors will be found.

Comments

It should be emphasized that, because of limitation of space, the foregoing discussion by no means includes a complete list of genetically determined gastrointestinal diseases. Also, in view of the relatively incomplete genetic knowledge concerning many gastrointestinal diseases, a complete listing is not possible. The reader who is particularly interested in this subject is referred to the several discussions and reviews which are available.

The subdivisions created for the purpose of this discussion are intended merely to facilitate exposition of some of the aspects of genetic gastrointestinal disease; they should not be construed as an attempt at fundamental classification. Some of those diseases which have been referred to in the literature as being due to single genes or a pair of genes (alleles) have had insufficient pedigree studies, and may be found eventually to be dependent for their penetrance on the presence or absence of other alleles. Often, the characterization of the inheritance pattern as dominant or recessive is based upon limited data. Also, the distinction between a disease of function and one of structure is frequently unclear. It seems likely that future investigations will demonstrate that deficiencies or anomalies of enzyme protein are involved in the causation of some structural gastrointestinal diseases.

Hereditary factors are seldom clear-cut. The collection of accurate pedigree data in the human is fraught with difficulties and errors because of insufficient numbers of offspring on which to base mathematical ratios, long generation time, illegitimacy, secrecy, and misrepresentation. Our clinical and laboratory techniques are often insufficient to recognize phenotypic abnormality. Undiagnosed in-utero lethality, new mutations, sex limitation, and intermediate gene action further becloud the data and confuse our interpretations. Heredity is to a greater or lesser extent concerned in the etiology of all diseases. However, there are few purely genetic diseases. Even those diseases predominantly determined by heredity are the product of the combined effect of several alleles, all of which are influenced by exogenous factors. The extent of the intricate and continuous interaction between the genotype and its environment obliges the genotype to play only a modified role in phenogenesis. The elucidation of that role is of vital concern to the gastroenterologist, whether he be working in the laboratory or the clinic.

(The references may be seen in the original article.)

PRESSURE BANDAGING OF THE LOWER EXTREMITY

USE AND ABUSE

Elias A. Husni, MD, Jose O. C. Ximenes, MD, and Frederick G. Hamilton, MD,
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Venous hemodynamic studies and phlebograms of the lower limb were undertaken in 35 patients and 16 controls when clinical conditions were identified with the use of pressure bandaging. It was demonstrated that pressure dressings around the knee caused severe compression of the popliteal veins and remarkable elevation of the peripheral venous pressure in the horizontal as well as the ambulatory limb. An air splint inflated to a pressure of 15 to 20 mm Hg offered excellent compression without compromising the deep circulation. The study strongly suggests that: (1) Pressure bandaging of the knee joint retards venous circulation and may contribute to thromboembolism. It should be abandoned in favor of the "G" splint. (2) For prophylaxis against thromboembolism, elastic bandages should stop below the knee joint.

The value of pressure dressings in establishing hemostasis and gentle splinting of wounds was recognized in the early days of surgery. Elastic bandages of various kinds and strengths replaced the old linen bandages to take an integral part in management of varicose veins, phlebitis and its complications, and in major surgery on the limbs, particularly the knee joint. The elastic bandage is probably one of the most widely used and abused items in medicine. Application of elastic bandages to the limbs is taken lightly by the physician and is usually delegated to the nurses. A well-applied bandage offers comfort, hemostasis, and improves venous return; on the other hand, a poorly applied bandage may do just the reverse and may predispose to phlebothrombosis and thromboembolism. The purpose of this study was to obtain data on venous circulation in the bandaged lower limb. The study was prompted by the occurrence of multiple episodes of thromboembolic phenomena in patients with firmly bandaged knees.

Methods

Phlebograms and hemodynamic studies of the lower limbs were undertaken in 51 patients of both sexes to investigate the three conditions usually associated with the use of elastic bandaging (Table 1), ie. varicose veins, acute phlebitis, and postphlebitic disease. A tributary of the great saphenous vein in the foot or ankle was cannulated with a gauge-18 plastic tubing and connected to a bottle of physiologic saline solution. The following studies were then carried out: The resting venous pressure (RVP), standing venous pressure (SVP), and ambulatory venous pressure (AVP) were measured with the patient in a supine position, standing position, and after ambulation, respectively. The AVP determination was made after the patient walked 200 feet at a rate of 120 steps per minute, or double-timed in place, at the same rate, for 40 seconds, or until the column of fluid in the tubing became stationary. The same determinations were then repeated in the control group of patients with an orthopedic-type pressure dressing around the knee joint, with and without elastic bandaging from the toes to the midthigh. Bandaging of the knee joint in this manner is ordinarily applied with a pressure of 25 to 30 mm Hg. This range was established by evaluating the pressure in 12 cases with a rubber balloon placed under the dressings and connected to a manometer.

Determinations of the RVP and AVP were repeated in the control group with the knee bandaged at 20, 15, and 10 mm Hg. Finally, the RVP was measured with the knee joint immobilized in a "G" splint inflated to pressures of 15, 20, and 30 mm Hg. Phlebograms were obtained in a horizontal position with and without the above elastic bandages and G splints. After the patients received 60 ml of 50 percent diatrizoate (Hypaque) sodium which was injected through the cannula by hand, two exposures, 15 seconds apart, were made of the lower limb during Valsalva's maneuver.

TABLE 1.—*Peripheral Venous Pressure in Both Patient Groups* *

Diagnosis	No. of Patients
Varicose veins	9
Acute phlebitis	10
Postphlebitic disease	16
Normal controls	16
Total	51

* Age of patients ranged from 19 to 83 years.

From the divisions of vascular and orthopedic surgery, Huron Road Hospital, Cleveland.
Reprint requests to 13951 Terrace Rd, Cleveland 44112 (Dr. Husni).

TABLE 2.—*Peripheral Venous Pressure Without Compression* *

	No. of Cases	Resting (RVP)	Standing (SVP)	After Exercise (AVP)
Control group	16	7.3±1.4	120±11	42±12.7
Varicose veins	9	8 ±1.8	120± 6.7	85±18.9
Acute phlebitis	10	21.1±9.5	122± 6.1	114±24
Postphlebitic	16	12.5±4.1	123± 5.8	114±23.7

* Mean pressure measured per centimeter of saline and standard deviation.

Results

The preliminary pressure determinations yielded data consistent with the underlying pathologic physiology (Table 2). The RVP was elevated in both acute phlebitis and postphlebitic disease. The same patients also displayed various degrees of ambulatory venous hypertension.

In the absence of obstruction to the venous return, the RVP is an expression of the vis a tergo of the arterial blood pressure. The SVP, on the other hand, is not affected by any pathologic state of the veins but varies directly with the individual's height and represents the pressure exerted by a column of blood from the level of the third intercostal space (middle of the right atrium) to the level of the foot. The ambulatory venous pressure (AVP), also measured in the erect position is a measure of the effectiveness of the musculovenous pump of the leg. The action of the contracting muscles upon normal veins propel the blood in only one direction, toward the heart. Consequently, the venous pressure at the ankle drops to a level varying between the midleg and migthigh, to at least 50 percent of the SVP. In the presence of impairment of the musculovenous pump the SVP fails to drop appreciably and a state of elevated ambulatory venous pressure ensues.

Application of pressure dressings around the knee joint with or without bandaging the entire leg effected a remarkable increase in the RVP in all cases, simulating a major venous occlusion. The AVP was also elevated, but to a lesser degree (Table 3). The parameters returned to normal only when the bandaging pressure approximated 10 mm Hg. In contrast, the G splint did not alter the RVP in a random sample of all groups (Table 4). Here the AVP could not be determined because the inflated splint immobilized the knee joint.

The phlebograms obtained with pressure dressing around the knee joint demonstrated severe compression of the normal popliteal vein in every case. This fact was undoubtdly responsible for raising both the RVP and AVP in these patients. The G splint, on the other hand, while compressing the

TABLE 3.—*Peripheral Venous Pressure in Controls and Patients With a Bandaged Knee* *

RVP		SVP	AVP	
Control Reading	Bandaged Knee		Control Reading	Bandaged Knee
6	30	117	45	60
5	26	114	38	50
10	30	109	60	71
7	30	124	40	62
6	42	121	40	48
8	39	114	60	75
8	42	120	55	55
8	36	110	58	68
8	40	134	20	20
9	30	154	Infiltrated	
7	36	124	52	52
7	30	115	27	85
5	30	110	Infiltrated	
7.2±1.4 †	34±5.2 †	120±11 †	45±12 †	58±16.4 †

* Measured in centimeters of saline.
† Mean pressure and standard deviation.

TABLE 4.—*Peripheral Venous Pressure With G Splint*

Patient Groups	Control Reading	Inflation Pressure of Splint 15-18 mm Hg	Inflation Pressure of Splint 30 mm Hg
Normal control	8	9	20
Normal control	9	10	16
Normal control	6	6	24
Normal control	8	8	24
Phlebitis	10	10	34
Postphlebitic	13	13	26
Postphlebitic	15	17	30
Varicose veins	12	12	30
Varicose veins	7	8	16
Varicose veins	13	14	26
	10.1±2.8 *	10.7±2.9 *	24.6±5.7 *

* Mean pressure (measured in centimeters of saline) and standard deviation.

varicose veins, did not appear to compromise the deep venous flow at the stated pressure. However, when the inflation pressure exceeded 20 mm Hg compression of the deep veins became apparent concomitant with a comparable rise in the RVP, approximately millimeter for millimeter (Table 4).

Comment

The role of stasis in the etiology of venous thrombosis was recognized nearly a century ago. Its clinical significance was probably the basis for the development of elastic bandaging of the lower limbs. Friedlander in 1935 and Ochsner in 1941 recommended pressure bandaging of the lower extremities in an attampt to prevent phlebothrombosis in postoperative patients. However, objective data relative to the effect of pressure bandaging upon the circulation in the lower limb were lacking. In 1954, Paulsen and his group demonstrated that the rate of venous flow in the lower extremity may be markedly increased by the application of an elastic compression bandage from the toes to just below the knee.

Although no mention was made to the pressure with which the bandages were applied, it was clear that the knee area was not compressed.

The data provided by this study attribute a tourniquet-like effect to firm bandaging of the knee joint even when the entire limb is wrapped. The peripheral venous pressure rose nearly five times that of control values (Table 3), and the phlebograms unmistakably demonstrated severe compression of the popliteal vein in every case. Obstruction of the popliteal vein was still in evidence until the elastic compression pressure was reduced to approximately 10 mm Hg. Although active exercise seems to significantly overcome the tourniquet-like effect of the pressure dressing as evidenced by the low AVP in this group, this cannot be assumed to occur in patients convalescing from surgery on the limb. These patients are not capable of the vigorous ambulation employed in this study, and will therefore undoubtedly maintain a significant degree of both RVP and AVP throughout the convalescent period. Obstruction of the popliteal vein in this manner undoubtedly contributes to phlebothrombosis in patients confined to bed as a result of illness or surgery and defeats the very purpose for which these bandages were conceived.

The use of the G splint, on the other hand, did not suggest any untoward effects on the venous circulation until the inflation pressure exceeded 20 mm Hg. This is undoubtedly due to the fact that, unlike elastic bandages, the air splint exerts a constant and uniform pressure throughout the length of the limb and does not permit folding or creasing with body movements. The use of an inflatable splint with a pressure of 15 to 20 mm Hg probably affords maximum venous acceleration with minimum inflow obstruction. It increases the linear velocity by decreasing the total cross-sectional area of the venous bed. The optimum pressure appears to be in the neighborhood of 20 mm Hg. Increase in inflation pressures beyond this level is associated with compression of the deep veins and an increase in the peripheral venous pressure (Table 4).

This study does not discredit the use of properly applied elastic bandages, but definitely suggests that when these are employed they should probably stop short of the knee joint. When the aim is to improve venous returns in the resting limb, no advantage may be gained by extending the compression bandages above the knee level. This may be a disadvantage, and the desired hemodynamic changes may indeed by reversed.

This study indicates that when the knee joint itself is concerned, local hemostatic compression bandages should be abandoned. As was intimated earlier, it was the occurrence of several cases of thromboembolic phenomena associated with pressure dressings around the knee joint that promoted this study. Granted that the phlebothrombosis may have predated the surgery on the knee and the pressure dressings, nevertheless, occlusion of the popliteal vein by the dressings as a causative factor cannot be ignored. Furthermore, desirable hemostasis and splinting of the knee joint should be undertaken without compromising the deep venous circulation. The G splint appears to be ideally suited for this purpose.

Generic and Trade Names of Drug

Diatrizoate sodium—*Hypaque Sodium.*

(The figures and references may be seen in the original article.)

MEDICAL ABSTRACTS

ABDOMINAL SURGERY

Claude E. Welch, MD, New Eng J Med 280(7):358–363, Feb 13, 1969, 280(8): 419-425, Feb 20, 1969 and 280(9): 480-487, Feb 27, 1969.

In common with previous reports, the last of which appeared two years ago, this paper summarizes recent important contributions to the knowledge of surgical diseases of the abdominal viscera. The flood of articles in this field has continued in an undiminished fashion, so that in many instances, contributions typical of a trend may be included, whereas others, for lack of space, must be omitted. Abstracts in general are brief, and designed to call attention to specific articles for details.

PROGNOSIS OF GENERAL PARESIS AFTER TREATMENT

E. Wilner, MD, and J. A. Brody, MD, Lancet II(7583): 1370-1371, Dec 28, 1968.

A follow-up of 100 patients with general paresis who had survived at least ten years after initial treatment revealed that at least 31% had had new signs of neurological disease subsequent to treatment. In 64 patients who received penicillin therapy, either alone or in combination with other therapy, 39% had new neurological signs. These rates are far in excess of those which would be expected by chance and are higher than those previously reported where duration of follow-up was much shorter.

HISTORY OF BLOOD TRANSFUSION: A TERCENTENNIAL LOOK

Peter Hutchin, MD, Surgery 64(3): 685–700, Sept 1968.

On April 17, 1668, by an edict of the French Parliament, the practice of blood transfusion was banned from the therapeutic armamentarium of the seventeenth century physician. This injunction followed the experiments of Jean Baptiste Denis of Paris very closely and halted further development of blood transfusion for the next 150 years. In 1818, James Blundell, a London obstetrician, revived interest in blood transfusion, but its general therapeutic use did not come for another 100 years. Unrecognized problems of immunological compatibility, unavailability of anticoagulants, and the lack of safe, aseptic, and practical methods of transfusion were the principal stumbling blocks that thwarted progress. After 1918, blood transfusion was gradually established as a practical procedure, but its meteoric rise began only with the establishment of blood banks just before World War II. Most recently, great strides have been made both in blood procurement and blood preservation.

Today, transfusion of blood is an integral part of medical practice; its history, however, is quite diverse and reflects the development and evolution of medical thought through the ages. It is therefore of great interest to retrace the early stages of blood transfusion and to view in retrospect the ideological and mental processes of our predecessors.

CIRCULATORY SHOCK

Max Harry Weil, MD PhD, Moderator, J Trauma 9(2): 140-156, Feb 1969.

Since 1963, an annual conference has been arranged in Los Angeles to acquaint physicians with new research developments relating to the mechanism and treatment of shock states. The symposium is designed to present practical applications for treatment of patients. The common occurrence of circulatory shock and the relative ineffectiveness of current modes of treatment attract physicians in almost every medical specialty. Within the last five years, significant advances have been made in the field. During this interval, extensive studies have been undertaken at the bedside of patients in shock, as well as in experimental laboratories.

Several clinical research centers for the specialized study of patients in shock are now in operation. The first of these to be established was the Shock Research Unit of the University of Southern California School of Medicine at the Los Angeles County General Hospital. The stimulus provided by this unit has been in part responsible for the increasing interest in treatment of shock and in other aspects of the care of the critically ill in the Los Angeles medical community. The fifth annual Symposium on Circulatory Shock, held on February 8, 1967, was attended by more than 500 physicians. The University of Southern California was honored by the participation of Francis D. Moore, M.D., known for his significant contributions to the understanding of metabolic, pulmonary and circulatory defects related to surgical trauma, and also by the presence of Lerner B. Hinshaw, Ph.D., who has devoted much of his career to the study of endotoxin shock. These guest speakers were among the visitors who supplemented the regular faculty of the University of Southern California School of Medicine, and in particular the staff of the Shock Research Unit.

SCHIZOPHRENIA

Norman Q. Brill, MD, Moderator, Ann Intern Med 70(1): 107-125 Jan 1969.

It seems increasingly likely that schizophrenia is a symptom complex of disordered thinking, feeling, and behavior rather than a single disease. While psychogenic factors seem to play an important role in most instances, no pattern of environmental and emotionally traumatic factors has ever been found

that would inevitably lead to the development of schizophrenia. It appears that hereditary, constitutional, and environmental factors contribute in varying proportions to the development of schizophrenic disorders. Observation of newborn infants suggests they are born with different temperaments and personalities that will react to the same stresses in different ways. The time in life (that is, the stage of development) when stress occurs is believed by many to be as important as the nature of the stress. Experiences that could be satisfactorily dealt with at age five or six might be traumatic and overwhelming at two or three.

Neurophysiologic and biochemical abnormalities that may be contributory (or concomitant) factors in schizophrenia will probably be defined as investigatory techniques as they are further developed. Suggestive findings have already been described in controlled studies of average-evoked auditory and visual-evoked brain potentials, and the Russian neuropsychiatrist Snezhnevsky, using a toposcope—a 50-channel electroencephalogram—has described a pattern of activity in schizophrenics that differs from normals.

Although new drugs have very helpful in the management of schizophrenic patients, present treatment methods leave much to be desired. As long as the causes of the illness are not known, treatment will continue to be empirical.

STRONGYLOIDIASIS AT THE BOSTON CITY HOSPITAL

H. Amir-Ahmadi, MD, et. al., Amer J Dig Dis 13(11): 959-973, Nov 1968.

Strongyloidiasis is primarily a disease of the tropics. Recent interest in this disease is due to the increasing frequency with which strongyloidiasis, a potentially fatal disease, is encountered in all parts of the world. In nontropical regions, where strongyloidiasis is less frequently encountered among the general population, institutions for mentally retarded children may comprise foci of this infection. Yoeli *et al.* reported recovery of *Strongyloides stercoralis* from 17.7% of 1453 severely retarded children in a New York State institution.

This paper reports a case of strongyloidiasis notable for prompt and apparently complete response to thiabenzadole (Mintezol) therapy in spite of a particularly intense infection. The presence of gastric achlorhydria and evidence for intestinal malabsorption were also documented in this patient. Favorable response to thiabenzadole therapy in 4 additional patients, presenting less severe symptoms from *Strongyloides* infection, are also reported.

THE HUMAN BODY BURDEN OF LEAD

H. A. Schroeder, MD, and I. H. Tipton, PhD, Arch Environ Health 17(6): 965-978, Dec 1968.

Concentrations of lead in human tissues from 33 cities of the United States and foreign countries were determined. Differences from place to place were observed, median values generally being higher in US subjects than in those from Africa, the Middle East, and in a few tissues, the Far East. Mean values of lead increased with age in US aortas, kidneys, bones, livers, lungs, spleens, and pancreases; in foreign tissues only aortic lead increased with age. Smooth, striated, and heart muscles and brain had little lead. Bone lead was higher in US subjects than in Far Easterners. Bone contained 91% of the total body lead.

At the time these samples were collected (1952 to 1957) the exposure of US subjects to lead from all sources was apparently large enough to cause accumulation with age, whereas in most foreign areas it was not. It is likely that atmospheric lead from motor vehicle exhausts largely accounts for increased exposures, and that inspired lead may make up a sizable portion of the total amount absorbed by the body.

Although experimental toxicity of lead in animals with tissue concentrations similar to those of human beings has been demonstrated, no clinical evidence of bizarre innate toxicity was discovered in these human subjects.

In human soft tissues, mean concentrations of lead were not found to displace any of the essential trace elements of low concentration: chromium, manganese, cobalt, copper, or molybdenum.

In view of the steadily increasing annual pollution of air and soils with lead from motor vehicle exhausts, innate toxicity in exposed human beings may appear.

HYPERTHYROIDISM

D. H. Solomon, MD FACP, Moderator, Ann Intern Med 69(5): 1015-1035, Nov 1968.

The hypothesis that uncoupled or loosely coupled oxidative phosphorylation is a fundamental abnormality in hyperthyroidism is no longer tenable. Rather, mitochondria from hyperthyroid muscle are increased in number but normal in phosphorylative behavior. Sarcotubular vesicles are also increased in amount and appear normal in biochemical function. The cause of muscle weakness remains unknown.

The clinical features of hyperthyroidism are reviewed, with personal observations on their usefulness in diagnosis. The syndrome of Graves' disease is defined as a tri-system disease (thyroid, eye, and skin), and the autoimmune hypothesis of its origin is discussed in the light of the properties of the long-acting thyroid stimulator (LATS), an immunoglobulin unique to Graves' disease.

The choice of treatment of hyperthyroidism is still a matter for controversy. It is agreed that subtotal thyroidectomy, radioiodine, and antithyroid drugs, all have a role in treatment, but opinions differ on their comparative usefulness in various types of patients.

CRYPTOCOCCOSIS: CURRENT STATUS

M. L. Littman, MD PhD, and J. E. Walter, DVM DRPH, Amer J Med 45(6):922-932, Dec 1968.

Cryptococcosis is a cosmopolitan infectious disease of many which begins as a primary infection of the lungs and which may spread to the central nervous system in susceptible subjects. The disease is encountered more frequently in patients with Hodgkin's disease, lymphosarcoma, leukemia and diabetes, and in those receiving prolonged therapy with steroids. Although the incidence of the disease in the United States is low, it is second to histoplasmosis as a cause of death by mycotic agents. The drug of choice for treatment of cryptococcal meningitis remains amphotericin B, the use of which has reduced mortality considerably. Specific toxic effects on the kidneys may be lessened by alternate day intravenous therapy and monitored more accurately by the creatinine clearance. The presence of the etiologic agent in the sputum in the absence of overt evidence of disease, indicates the existence of a carrier state in men. Circulating cryptococcal antigens are present in the serum and spinal fluid in the active phase of the disease and decline during the recovery phase when circulating antibodies appear. Although skin testing antigens have been improved, an adequate antigen is still unavailable. Since normal human serum inhibits the etiologic agent, changes in the anticryptococcal activity of the serum which appear as sequelae of debilitating disease, therapy with steroids or other immunosuppressive agents may be a prime factor in the development and course of cryptococcosis. Avian habitats, especially those of the pigeon, furnish a prime source of human and animal infection. The pigeon has been shown to be moderately susceptible to experimental infection with C. neoformans and to carry the organism mechanically on its beak and feet, although spontaneous infection has not yet been demonstrated. The excreta of pigeons and other birds has been shown to be a rich source of C. neoformans. Pigeon handlers have been found to have a much higher incidence of cryptococcal antibodies than nonhandlers. Measures for the prevention of cryptococcosis included the control of pigeons and decontamination of pigeon sites.

RESEARCH SECTION

LIST OF RECENT PUBLICATIONS FROM RESEARCH LABORATORIES

The following papers have been completed by research activities under the direction of the Bureau of Medicine and Surgery.

Naval Air Development Center:

"A Method and Rating System for Evaluation of Thermal Protection," by Alice M. Stoll and Maria A. Chianta. NADC-MR-6809, Dec 2, 1968.

Naval Aerospace Medical Institute:

"Base-line Blood Determinations of the Squirrel

Monkey *(Saimiri sciureus),"* by Albert E. New. *The Squirrel Monkey,* Academic Press, Inc., 1968.

"Comparative Evaluation of the Radiation Environment in the Biosphere and in Space," by Hermann J. Schaefer. NASA-NAMI Joint Report, Dec 1968.

"Evaluation of Sixteen Anti-motion Sickness Drugs Under Controlled Laboratory Conditions," by Charles D. Wood and Ashton Graybiel. *Aerospace Medicine* 39(12), Dec 1968.

"Factor Analysis of Aviation Training Measures and Post-Training Performance Evaluations," by Richard F. Booth and James R. Berkshire. NAMI-1050, Oct 1968.

"The Somatic Chromosomes of the Mogolian Gergil *(Meriones unguiculatus),"* by Steven P. Pakes. NASA-NAMI Joint Report, Jan 1969.

"The Squirrel Monkey in Aerospace Medical Research," by Dietrich E. Beischer. *The Squirrel Monkey,* Academic Press, Inc., 1968.

Naval Medical Field Research Laboratory:

"Body Armor in a Hot Humid Environment, Part II: Studies in Heat Acclimatized Men," by W. E. Yarger. B. D. Litt & R. F. Goldman. NMFRL Report XIX(1), Jan 1969.

"Development of the NMFRL Telemetry System, Second Report," by Wade G. Holcomb, and Philip J. Rasch. NMFRL Report XIX(2), Jan 1969.

"Evaluation of the Purity Water Filter," by Ned S. Hurst. NMFRL Report XIX(3), Feb 1969.

Naval Medical Neuropsychiatric Research Unit:

"Prognostic Indicators in Psychosis and Neurosis," by E. K. Eric Gunderson and Ransom J. Arthur. *Journal of Abnormal Psychology* 73(5), 1968.

"Serum Uric Acid and Cholesterol Variability: A Comprehensive View of Underwater Demolition Team Training," by Richard H. Rahe, Robert T. Rubin, Ransom J. Arthur, and Brian R. Clark. *Journal of the American Medical Association* 206, Dec 23, 1968.

Naval Radiological Defense Laboratory:

"Effect of X Irradiation (0.6-2.4kR) on Cation Activated Atpases from Subcellular Fractions of Rat Brain," by J. T. Cummins and B. E. Vaughan. NRDL-TR-68-128, Nov 12, 1968.

"Modification of Urethan-Lung Tumor Incidence by Low X Radiation Doses. Cortisone and Transfusion of Isogenic Lymphocytes," by L. J. Cole. NRDO-TR-69-1, Dec 30, 1968.

Naval Medical Research Institute:

"Influence of Gas Environment on Catabolic Activities and on Reoxidation of Reduced Nicotinamide Adenine Dinucleotide Phosphate in Chlamydia," by E. Weiss, E. M. Neptune, Jr., and R. W. Gaugler. *Journal of Bacteriology* 96(5), Nov 1968.

"Fetal Heart Studies with the Ultrasonic Doppler Technique," by Richard L. Bernstine. *American Journal of Obstetrics and Gynecology* 102(7), Dec 1, 1968.

"Hematozoa From Mammals of South Vietnam," by P. F. D. Van Peenen, Harry Hoogstraal, J. F. Duncan, and P. F. Ryan. *J Protozool* 15(3), 1968.

"The Interaction of Mercurials with Helical and Random Polyuridylic Acid," by David B. Millar. *Biochem Biophys Acta,* Vol 166, 1968.

"Interferon Induced by Plasmodium berghei," by Kun-Yen Huang, Warren W. Schultz, and Francis B. Gordon. *Science,* Vol 162, Oct 4, 1968.

"Lack of Deoxyribonucleic Acid Homology Between Species of the Genus *Chlamydia,"* by David T. Kingsbury and Emilio Weiss. *Journal of Bacteriology* 96(4), Oct 1968.

"Modification of Meningococcal Polysaccharid Antigens for Use in Passive Hemagglutination Tests," by B. W. Hammond, D. T. Kingsbury, and Emilio Weiss. *Journal of Immunology* 101 (4), 1968.

"Production of Interferon in Mice: Effects of Altered Gaseous Environments," by Kun-Yen Huang and Francis B. Gordon. *Applied Microbiology* 16(10), Oct 1968.

"Public Health Aspects of Galactic Radiation Exposure at Supersonic Transport Altitudes," by Hermann J. Schaefer. *Aerospace Medicine* 39 (12), Dec 1968.

"Sensory Deprivation (Sleep Saturation?) and Performance," by Thomas I. Myers. NMRI Research Report No. 2, Oct 1968.

"The Sporogonous Cycle of Plasmodium Vivax in Anopheles Mosquitoes as a System for Evaluating the Prophylactic and Curative Capabilities of Potential Antimalarial Compounds," by L. A. Terzian, N. Stahler, and A. T. Dawkins, Jr. *Experimental Parasitology* 23(1), Aug 1968.

"Stimulation of Osteogenesis in the Dog Mandible by Autogenous Bone Marrow Transplants," by H. E. Richter, Jr., W. E. Sugg, Jr., and P. J. Boyne. *Oral Surgery, Oral Medicine, and Oral Pathology* 26(3), Sept 1968.

"Studies on Nuclear Division of a Malarial Parasite Under Pyrimethamine Treatment," by Masamichi Aikawa and Richard L. Beaudoin. *Journal of Cell Biology* 39(3), 1968.

"A Temperature-Controlled Feeding Apparatus for Hematophagous Arthropods," by A. C. Pipkin and T. J. Connor. *Journal of Medical Entomology* 5(4), 1968.

"Toxic Effects of Carbon Dioxide and Ternary Nitrogen-Oxygen-Carbon Dioxide Hyperbaric Atmospheres on the Work Function of Cholinergic Tissues," by S. L. Friess, R. C. Durant, P. L. Andrus, and H. B. Weems. *Toxicology and Applied Pharmacology,* Vol 12, 1968.

Naval Medical Research Unit No. 1:

"Enhancement of Mengovirus Nucleic Acid Infectivity by Putrescine," by A. B. Cobet and T. G. Akers. *Applied Microbiology* 16(8), Aug 1968.

"Statolon-Induced Resistance of Mice to Lethal Aerosols of Columbia-SK Virus," by T. G. Akers and B. D. Stirling. *Proceedings of the Society for Experimental Biology and Medicine,* Vol 128, 1968.

Naval Medical Research Unit No. 2:

"Contributions of Copper Balance Studies to Investigation and Management of Wilson's Disease," by Raymond H. Watten, Jun-Bi Tu, R. Quentin Blackwell, and Tsung-Yung Hou. *Birth Defects Original Article Series* IV(2), April 1968.

"A Controlled Retrospective Study of Blackfoot Disease, an Endemic Peripheral Gangrene Disease in Taiwan," by I-Cheng Ch'I and R. Quentin Blackwell. *American Journal of Epidemiology* 88(1).

"Diagnosis and Treatment Studies of Patients in Asymptomatic Stage of Wilson's Disease," by Jun-Bi Tu, R. Quentin Blackwell, James W. Fresh, and Raymond H. Watten. *Birth Defects Original Article Series* IV(2), April 1968.

"Haemoglobin E. in Chinese," by R. Quentin Blackwell, Hung-Ju Yan, Chen-Sheng Liu, and Chieng-Chang Wang. *Trop Geogr Med,* Vol 20, 1968.

"Hemoglobin Variant Common to Chinese and North American Indians," by R. Quentin Blackwell. *Science,* Vol 161, July 26, 1968.

"Incidence of G-6-P D Deficiency and Hemoglobin H. Among Filipinos," by R. Q. Blackwell, A. A. Paraan, Jeanette T. -H. Huang, L. Yen, and L. -C. Chien, *Vox Sanguinis,* Vol 15, 1968.

"New Species of Mosquitoes from Taiwan (Diptera: Culicidae)," by Jih Ching Lien. *Tropical Medicine* (Part I) 9(4), Dec 1967, (Part II) 10(1), Mar 1968, (Part III) 10(2), Sept 1968, and (Part IV) 10(3), Nov 1968.

Naval Medical Research Unit No. 4:

"Identification of Neisseria Meningitidis Carbohydrate Fermentation Patterns in Mueller-Hinton Booth," by D. W. Beno, L. F. Devine, and G. L. Larson. *Journal of Bacteriology* 96(2), Aug 1968.

"Prophylaxis of Acute Viral Respiratory Disease with Gamma Globulin," by M. W. Rytel, J. M. Dowd, E. A. Edwards, W. E. Pierce, and J. H. Pert. *Diseases of the Chest* 54(6), Dec 1968.

Naval Submarine Medical Research Center:

"Conservative Management of Mandibular Incisors with a Large Area of Bone Involvement," by J. L. Giunta and Bruce W. Wisner. SMC Memorandum Report 68-8, April 16, 1968.

"Consideration of Some Hi-Fi Earphones for Submarine Sonar," by Alan M. Richards. SMC Memorandum Report No. 68-14, July 30, 1968.

"Saturation-Excursion Diving: Biochemical Cycle Functions in Lactic Dehydrogenase, Lactate, and Pyruvate Responses," by K. E. Schaefer, J. J. Jacey, C. R. Carey, and W. F. Mazzone. SMC Report No. 536, June 18, 1968.

"Stress Response in Chronic Hypercapnia," by Karl E. Schaefer, Nancy McCabe, and Judith Withers. SMC Report No. 524, May 16, 1968.

"A Systems Analytical Approach to Assessment of Human Reliability," by Benjamin B. Weybrew and Jack L. Kinsey. SMC Memorandum Report No. 68-15, Sept 30, 1968.

HOSPITAL ADMINSTRATION SECTION

HOSPITAL ADMINISTRATION NOTES

Selected Publication: The Packaged Disaster Hospital, Improved Mass Casualty Care,—a packaged Disaster Hospital (PDH) consists of supplies, equipment and pharmaceuticals packed for long-term storage. In disaster, it can expand the hospital to which it is assigned or be set up as a separate 200-bed hospital. This profusely illustrated book, issued by the Division of Health Mobilization, U.S. Public Health Service provides general guidance for hospital staffs with which PDH's are affiliated, presents information for hospitals considering application for PDHs and serves as a text for organizations sponsoring disaster training courses. It deals primarily with preparing for PDH use following nuclear attack. Stressed is the fact that planning for the ultimate disaster results in prepardness for the lesser but more likely catastrophe—flood, hurricane, earthquake, fire and major accident. 1967, 304 p. il. FS2. 302:D-6 price: $1.75 available from Government Printing Office, Washington, D.C. 20402.

Ration Data. Ration statistics for total hospital food service program during month of February 1969 are as follows: (Source—Food Service Performance Analysis, NAVMED 1412)

Total rations served	458,070
Total cost of provisions	$606,109.98
Average cost of ration (raw food or net cost)	$1.323
Average cost of whole, fresh milk/gallon	$0.81
Average ounces served whole, fresh milk/gallon	27
Percentage of Total Expenditures for:	
Meat, fish and poultry	38%
Whole, fresh milk	14%
All other categories	48%
Average ration cost for hospitals, by group:	
Group A (CONUS) 25,455 to 67,986 rations served	$1.310
Group B (CONUS) 9,643 to 18,829 rations served	1.295
Group C (CONUS) 2,999 to 10,559 rations served	1.367
Group D (OCONUS) 2,779 to 23,718 rations served	1.379
Average % of attached inpatients served	77%
Average % of attached staff/support personnel served	63%
Average % of modified diets to total inpatients served	16.4%
Average % of total expenditures for supplemental nourishments	2.5%

Food Sanitation. Retention of patient tray served but unopened food packets/packages for re-service to consumers is a questionable practice, considering the dangers of cross-infection hazards involved. It is recommended that all foods served and returned on patients' tray be destroyed to prevent possible reissue.

DENTAL SECTION

CONSERVATIVE MANAGEMENT OF MANDIBULAR INCISORS WITH A LARGE AREA OF BONE INVOLVEMENT

LT John L. Giunta, DC USNR and
LT Bruce W. Wisner, DC USNR.

A case report is presented in which a submariner's dental condition presented a choice between (1) extraction of the lower anterior teeth and (2) extensive root canal fillings and wide removal of cystic material around these teeth. The man was an FBM crew member soon to go on patrol. The conservative root canal treatment was elected, even though this meant that stabilizing wires had to be in place during the patrol to hold the loose teeth in place. This case illustrates that the isolation of an FBM patrol does not

The opinions and assertions contained herein are those of the authors and are not to be construed as reflecting the views of the Navy Department or the naval service at large.

necessarily preclude such extensive dental treatment in selected cases.

(Abstract by Research Work Unit MR005.19-6024.02 by LT John L. Giunta, DC USNR, and LT Bruce W. Wisner, DC USNR.)

CLINICAL USE OF ADDENT 12

W. R. Scott and R. H. Roydhouse, Dent Abs 14(3): 162-163, Mar 1969.

Addent 12, an esthetic, composite resin restoration material containing fine particles of lithium silicate as a filler, is a useful addition to the list of dental restoratives. In the author's clinical experience, Addent 12 gives good service when used as described. It may produce poor results if improperly handled.

Addent 12 is suitable for Class I pit and fissure cavities, Class III proximal cavities, and Class V gingival cavities. Pin-reinforced Class IV compositive restorations can also give limited service. Used with stainless steel pins, Addent 12 is superior to other materials for the restoration of teeth with vital pulps, intended as bridge abutments.

The wetting or spreading qualities of composite materials tend to diminish marginal penetration but do not eliminate the need for adequate mechanical retention. This is achieved readily with shallower retention walls and larger surfaces than are permissible for amalgam or gold restorations.

Addent 12 has inadequacies, especially in the nature of the surface finish and in the number of air bubules the mixed composite shows. Better lining methods and knowledge of its effects on the pulp would be desirable.

Three materials presently available have a similar synthetic resin base but differ in filler content. Addent 35 (also marketed by Minnesota Mining and Manufacturing Company) contains glass beads as a filler. Restorations of Addent 35 do not match the color of teeth in which they are inserted; many of these restorations darken and discolor within six months. Dakor (L. D. Caulk Company) is a mixture of base with beads and calcific minerals. Dakor, in the author's experience, varies in consistency and sets rapidly; the failure to control the setting of this material has made its clinical use impractical.

Addent 12 must never be packed like amalgam or silicate cement. The material is teased into the cavity. Manipulation should cease when a firmness of gel is detected. The setting mass need not be subjected to pressure. Addent 12 should be trimmed with carbide steel burs because the abrasive nature of the material rapidly blunts carbon steel burs.

(Scott, W. R. and Roydhouse, R. H. 925 West Georgia Street, Vancouver, British Columbia, Canada. Clinical use of a compositive restorative. J Canad Dent Assn 34: 469-475, Sept 1968.)

PSYCHOLOGICAL FACTORS IN PREVENTIVE DENTISTRY

Richard J. Cassidy, Dent Abs 14(3): 185-186, Mar 1969.

The philosophy and practice of preventive dentistry is the only available solution to the growing incidence of oral disease. To make preventive dentistry work, significant social changes must be achieved by members of the profession as well as by the general public.

These changes will be the dentists' perceptions, skills, and practices. Policy makers who would direct changes in these areas must understand the psychological factors influencing them.

The Decision Research Corporation has been conducting a study with the U.S. Army Institute of Dental Research under the sponsorship of the U.S. Army Medical Research and Development Command. The study aims at developing more effective procedures for communicating with a troop population regarding the needs for oral care and motivating them to a regular practice of oral self-care. Early in the study, it was realized that there was an equally important need to communicate with the dentists regarding the requirements and procedures of preventive dentistry in general and of oral health education in particular.

Among the general population the most relevant psychological factors lie in the lack of recognition of the possibility of preventive dentistry, the social and personal meanings of teeth, and attitudes toward dentistry, dentists, and dental care which serve as communicative blocks.

Among members of the profession, procedures are needed whereby the practitioner, student, or educator can perceive himself in relation to the mission of dentistry as having the capacity to effect results within this context. There is a need for continuing professional policy seminars to involve all members of the profession in inventing, implementing, and evaluating preventive procedures at all levels of practice.

(Cassidy, Richard J. Decision Research Corporation, 505 Fifth Avenue, New York 10017. Psychological factors in preventive dentistry. Alabama J Med Sci 5: 358-369, July 1968.)

LIMITATIONS OF PANORAMIC RADIOGRAPHY

Kenneth O. Turner, Dent Abs 14(3): 186-187, Mar 1969.

A radiographic film when properly processed with full development at the prescribed time and temperature, should provide (1) proper density and contrast, (2) minimal distortion of the object projected on the film, and (3) complete inclusion of the anatomic region to be examined. These requirements should be accomplished with a minimum of difficulty to the patient and the operator and with the least possible exposure to radiation. Such requirements would seem to argue in favor of the single-exposure panoramic projection as opposed to 12, 14, or 20 intraoral periapical projections. The author's experience with the Panorex suggests that oral panography is a valuable and simplified procedure which can supply helpful and even essential information in a variety of situations encountered in daily dental practice. However, lack of clarity of the image projected on the film contraindicates complete reliance on this procedure when image sharpness is essential, as it usually is.

Oral panography may be most helpful and informative as a supplement to routine intraoral procedures or as a screening method to be supplemented by intraoral or definitive extraoral views.

No single technic for providing all essential infomation in the field of oral radiography is available. Oral panography is no exception. It is an adjunct and not a complete replacement for a variety of technics to help acquire more accurate information and thus to permit better dental care for more people.

Systemic diseases that show abnormal changes in the oral hard tissues provide a favorable field for panoramic radiography.

(Turner, Kenneth O. 925 West 34th Street, Los Angeles, Calif. Limitations of panoramic radiography. Oral Surg 26: 312-320, Sept 1968.)

THE USE OF A CAVITY VARNISH UNDER DIRECT FILLING GOLDS

Eugene D. Voth and Oliver H. Scheideman, JS Calif State Dental Assn 36(5): 197-199, May 1968.

Three types of direct filling golds (foil cylinders, mat, and powdered) were used according to the manufacturers' directions. The cavity varnish used was Copalite. Teeth, cavity preparations, and instrumentation were standardized as nearly as possible, and the autoradiograph method discussed by Phillips and co-workers was used to observe marginal penetration. The degree of leakage was evaluated on a scale of 1 through 4 according to severity of leakage. Specimens restored with cohesive gold foil only showed very little marginal leakage, and this appeared to be slightly reduced when cavity varnish was used. Specimens with mat gold showed gross leakage, but two coats of Copalite significantly reduced this marginal leakage. Powdered gold specimens showed a slight amount of marginal leakage, which appeared to be reduced by placement of the varnish. In the specimens without varnish, the highest amount of leakage occurred around mat gold, and the greatest reduction of marginal leakage was noted in specimens of mat gold with varnish.

(Abstracted by: CAPT Nelson W. Rupp, DC USN, Ret.)

THE STRENGTH OF DENTAL AMALGAM AS INFLUENCED BY PINS

Robert E. Going, Joseph P. Moffa, George W. Nostrant and Bruce E. Johnson, J Amer Dent Assn 77(6): 1331-1334, Dec 1968.

To study the effect of pins on the compressive and tensile strengths of amalgam, dental amalgam was condensed in steel dies and stored at room temperature for 1 week before testing. Ten specimens were prepared for each combination of the factors to be tested—size of specimen, shape of pin ends, and orientation of pins to direction of force. The proportioning, triturating, and condensing of amalgam were standarized, as were all materials and equipment. Stainless steel threaded wire was used for the pins. Pins with wedge-shaped ends were cut with Starlite "Grip Snip" pliers and pins with flat ends were cut with a Whaledent "Dial-A-Pin Cutter."

For compressive strength tests, specimens were prepared in 4 x 8 mm dies with one 6-mm pin, and

in 6 x 12 mm dies both with one and with four 10-mm pins. For tensile strength tests, specimens were prepared in 4 x 8 mm dies with one 4-mm pin and in 4 x 12 mm dies both with one and with three 4-mm pins. Only flat-ended pins were used in the large dies, in which specimens were prepared with all pins parallel, diagonal, or perpendicular to the anticipated tensile stress. Specimens without pins served as controls for each factor tested.

Tests were made with an Instron testing machine at a loading rate of 0.05 cm/min. Compressive strengths were determined by loading specimens parallel to the long axis until failure occurred. Results revealed no significant differences between specimens as a result of size, presence or absence of pins, number of pins, or shape of the pin ends. Tensile strengths were determined by the diametral-compression method described by Sweeney and Burns, and all data obtained were subjected to analysis of variance at the 99% confidence level. Results showed no significant differences between specimens of different sizes, with differently shaped pin ends, or with pins parallel to the tensile stress. There was, however, a significant decrease in tensile strength when pins were perpendicular or diagonal to the stress. It was concluded that pins do not increase the compressive strength of dental amalgam but do decrease its tensile strength if they are perpendicular or diagonal to the direction of stress.

(Abstracted by: CAPT Nelson W. Rupp, DC USN, Ret.)

IMPROVED ORAL CYTOLOGIC SAMPLING BY MEANS OF DEEP SUCTION ABRASION

Paul Scheman, Harry Lumerman, and Lyn Altchuler, Waldemar Med Res Foundation, Inc, Woodbury, New York, OS OM OP 26(4): 505-513, Oct 1968.

Diagnosis of oral cancer by means of cytologic study has been criticised because of a high incidence of false negatives. It is thought that false negatives may be due in part to the fact that the cells obtained in most oral cytologic techniques are usually from the most superficial layers of the epithelial surface. An instrument called a Cytoaspirator has been designed to obtain cells from the deeper layers of the oral epithelium. The yield of cells obtained by this instrument are compared with that obtained by the more conventional tongue-blade technique. The tongue-blade method did not produce a single sample that included basal cells, whereas the Cytoaspirator method failed to do so in only two cases out of nine. Moreover, the average of the percentage of parabasal cells produced by the Cytoaspirator was more than twice as great as for the tongue-blade method. There was also noted an apparent correlation between a shift in the differential cell count and the progression of such clinical changes as inflammation, hyperplasia and hyperkeratosis.

(Abstracted by: CAPT George H. Green, DC USN.)

PERSONAL HABITS AND DIET IN RELATION TO PERIODONTAL HEALTH AND ORAL HYGIENE STATUS IN SUBMARINERS

LT August D. Kropp, MC USNR, and CDR William R. Shiller, DC USN.

Some previous reports indicated that submarine crewmen eat abnormally high amounts of carbohydrates and that their diet habits include many between meal snacks. If true, these facts would lead one to expect great oral health problems in submariners; particularly in those on patrol for long periods. A detailed dietary and oral health study was done aboard the USS NATHAN HALE (SSBN 623) to evaluate the problem.

The findings essentially disprove the previously reported beliefs. It was found that the FBM crew ate an essentially well rounded diet with only a moderate amount of between meal snacking.

(Abstract by Research Work Unit MR005.19-6064.03 by LT August D. Kropp, MC USNR, and CDR William R. Shiller, DC USN.)

The opinions and assertions contained herein are those of the authors and are not to be construed as reflecting the views of the Navy Department or the naval service at large.

CALCULUS FORMATION RATE IN MEN LIVING IN A SUBMARINE ENVIRONMENT

LT L. W. Piebenga, MC USNR, and CDR W. R. Shiller, DC USN, Dent Abs 14(2): 111, Feb 1969.

About 1% carbon dioxide in the closed atmosphere of a submarine does not alter the rate of dental calculus formation in young men.

Calculus formation rates were evaluated in men living in the closed, elevated CO_2 environment of a submarine. These rates were compared with values obtained in the same subjects before submarine patrol duty. The standardized Mylar foil technic was used to collect calculus from the mandibular anterior

teeth. Analysis revealed no significant differences between the prepatrol and patrol values.

Submarine personnel and the dental clinicians caring for them have voiced the opinion from time to time that calculus formation seems more rapid during a Polaris patrol compared with offpatrol periods. That opinion is now revealed to be without foundation.

(Piebenga, L. W. and Shiller, W. R. Submarine Squadron TEN, Fleet Post Office, New York. Dental calculus formation rate in a submarine environment. J. Dent Res 47: 613-615, July-Aug 1968.)

PERSONNEL AND PROFESSIONAL NOTES

CAPT GORDON H. ROVELSTAD BECOMES VICE PRESIDENT OF THE INTERNATIONAL ASSOCIATION FOR DENTAL RESEARCH

CAPT Gordon H. Rovelstad, DC USN, Officer in Charge of the Naval Dental Research Institute, Naval Training Center, Great Lakes, Illinois, was installed as the Vice President of the International Association for Dental Research at the organization's 47th annual meeting which was held in Houston, Texas, from 20 to 23 March 1969. In addition to this honor bestowed on a naval officer, the staff of the Naval Dental Research Institute presented six scientific papers dealing with subjects ranging from attempts to produce a vaccine against dental caries to development of new office and equipment designs to be used in delivery of dental care in the Navy.

This annual meeting of dental research scientists attracted participants from nearly all nations throughout the world. Over 2,500 persons were in attendance and some 700 scientific papers were presented. Of these, 31 were from Navy research programs. One of the outstanding Navy contributions was the demonstration of the results of utilization of an electron microprobe, which is capable of measuring directly in tooth enamel, without previous chemical treatment, floride concentrations down to 50 parts per million. This advance in technology will enable dental researchers to assess the three-dimensional distribution of fluorine in enamel. This implies better understanding of actions to inhibit dental caries. Optimization of fluoride therapy programs may now be undertaken.

COMPLETION OF EVALUATION QUESTIONNAIRES

The Naval Dental Research Institute, Great Lakes, Illinois, has been conducting a clinical evaluation of the long term effects of indirect pulp capping procedures in naval personnel. Evaluation questionnaires were inserted into the dental records of patients who had received this treatment. This survey is now terminated, and all outstanding questionnaires should be completed and returned to Pathology Division, Naval Dental Research Institute, Naval Training Center, Great Lakes, Illinois 60088.

NURSE CORPS SECTION

ORIENTATION PROGRAM FOR JAPANESE NURSES

Navy nurses frequently become interested in the nursing activities of their counterparts while stationed at overseas hospitals. Visits to local hospitals and sharing professional information, books and magazines stimulate a desire to do more. The Navy nurses stationed at the Naval Hospital, Yokosuka, Japan recently took part in a one week orientation program for Japanese nurses. It is described in the following article submitted by Captain Romaine M. Mentzer, NC USN, Chief of the Nursing Service.

A program for Japanese nurses was instituted at the Naval Hospital, Yokosuka, Japan on March 17, 1969. This program included a period of observation and orientation to the Naval Hospital, its function,

operation and mission. The participants were graduate Japanese nurses from the Naval Self Defense Hospital at Kurihama, Japan. All participants held supervisory positions in their native hospital.

The program was put into effect upon a suggestion from Admiral Matsuda of the Japanese Navy and Commanding Officer of the Naval Self Defense Hospital. He felt that an intrapersonal contact between the two hospitals would be a beneficial and educational experience. Our Commanding Officer, Captain Errion, was in agreement. We then proceeded to make plans to set up a program.

We were limited by the one week time allotted for the program for each group of nurses. We were uncertain as to the number of Japanese nurses in each group. One week prior to their arrival, we were notified that only two nurses would comprise the group each week, and that the total program would extend over a three week period of time.

Armed with this information, we made our plans. We formed a list of interpreters available from our staff. We then mapped out the following program.

First Day:	Period of orientation to the program, followed by a tour of the hospital. The remainder of the day was to be spent in observation of CSSR and its method of operation.
Second Day:	Operating Room
Third Day:	Intensive Care Unit
Fourth Day:	A surgical and an Orthopedic Ward
Fifth Day:	Physio-therapy Department. The afternoon was to be devoted to a discussion and evaluation of the program, followed by a social hour in the Chief Nurse's office.

On the morning of March 17, 1969, the first group of two Japanese nurses arrived, accompanied by their chief nurse. The immediate and obvious obstacle to the program was the language barrier. The Japanese nurses did not speek or understand English. We, of course, were in similar straits with the Japanese language. We could return their bow and greet them with one familiar Japanese phrase, "Ohayo Gozaimasu" (good morning). Beyond that, we were incommunicado until our interpreter arrived.

Accompanied by an interpreter, we then followed our schedule as planned. We had altered our staff so that a cordial and receptive atmosphere was encountered throughout our tour and did much to put our guests at ease. At the end of the first day, they seemed a little more relaxed, and hopefully, looked forward to returning the next few days.

Our first impression was that the Japanese nurses appeared timid, somewhat frightened, and, perhaps, doubtful about the whole program. Gradually they lost their timidity, began to ask questions, and actually participated in many of the nursing procedures. At times, there was much giggling over a mutal inability to communicate during the absence of an interpreter. During these times, sign language and the acting out of a situation proved to be not only amusing, but adequate and established a friendly bond between the participants.

An evaluation of the program took place in the afternoon of the last day. We were concerned because the short period of time allotted each group prevented us from developing a more detailed program. We were anxious to learn of their reactions to the program.

Through an interpreter, we then exchanged ideas and questions: Did we contribute anything to their edification? Was the program beneficial? Did they feel the time was adequate for their purposes? Would they have preferred to spend more time in one particular department, such as Intensive Care Unit? Could we have included more in the program? If so, what would they like us to have included?

The general concensus of opinion was that they considered the program an interesting and rewarding experience. Since they were all graduate nurses, they felt the period of time for observation was sufficient. They were particularly interested in the intensive care unit since their Admiral was interested in establishing such a unit in their hospital. They were most impressed by all our disposable supplies and sophisticated equipment.

The Japanese nurses commented on the efficiency and training of the ward corpsmen. They expressed a desire to send some of their orderlies to our hospital to observe and work along with our corpsmen. They felt that this might motivate their male attendants who considered tending the sick to be "Women's Work."

Coffee and cookies were served during a social hour in the chief nurse's office. The American Navy Nurses and the Japanese Nurses exchanged questions and displayed an interest in each others training and education.

In conclusion, we felt that the program had considerable merit. Our Japanese counterparts now feel more of a kinship with the American nurses. We plan to tour their hospital in the near future and are looking forward to meeting again.

OUTSTANDING YOUNG WOMEN OF AMERICA — NAVY NURSES

Thirteen Navy nurses were among those selected for inclusion in the forthcoming publication of Outstanding Young Women of America. They are:

LCDR Mary E. Baker
LCDR Joan C. Bynum
LCDR Mary K. Meehan
LCDR Dorothy Ann Yelle
LT Patricia Ann Bohuslav
LT Constance E. Frisbie
LT Sandra A. Kirkpatrick
LT Donna Yukiko Kishi
LT Virginia Mary Krall
LT Ann Langley
LT Kathleen M. Reardon
LT Beverly E. Teagle
LTJG Nelda Ann O'Neil

Most of those chosen have served or are now serving on Hospital Ships or in DaNang. In addition many have had duty as Nurse Programs Officers at Navy Recruiting Stations throughout the country.

The purpose of the publication of Outstanding Young Women of America is to recognize and honor the truly outstanding young women of the United States by focusing attention on their capabilities and capacity for progressive action. Selections are made on an impartial basis by local women's clubs throughout the United States, college alumni associations and the military services.

AEROSPACE MEDICINE SECTION

WHAT'S NEW IN PROTECTIVE CLOTHING?

The following articles present an informative discussion of the status of new protective clothing for Navy/Marine Corps aircrew personnel, and should prove useful to Flight Surgeons and Aerospace Physiologists in their lectures to flight personnel. At a recent meeting of APSET (Aviation Personal and Survival Equipment Team), the need for widespread and continued education of flying personnel relative to protective and safety equipment was emphasized. The publication of these articles, and others in the future, is in support of this APSET recommendation. It is hoped that personnel in the field will also contribute to the educational program and submit appropriate articles for dissemination through this media.

A REVIEW OF FIRE-RESISTANT FLIGHT CLOTHING DEVELOPMENTS FOR AIRCREWMEN

Lionel I. Weinstock, Crew Systems Division, Naval Air Systems Command.

The Navy has played a pioneering and major role in the development and Fleet introduction of inherently fire-resistant flight clothing for aviation personnel. This clothing has proven to be effective in preventing and reducing serious burn injuries associated with accidental aviation fires. The expanding use of materials and clothing of this type by the U.S. Air Force and U.S. Army, to protect against the hazards of aircraft fires, has attested to their growing confidence in following the Navy's approach in meeting this ever present hazard to military airmen.

This article reviews the background of these developments, discusses the properties and advantages of the new materials, and summarizes the Navy's present and future fire-resistant protective flight clothing program.

Background

As early as 1957 the NAVAIRSYSCOM and its scientists at NAVAIRDEVCEN (Naval Air Development Center) recognized the merit of exploring the full potential of "Nomex", a then experimental high-temperature resistant fiber developed by the Dupont Company. The Navy was not entirely satisfied with the performance of its existing flight clothing materials and their ability to protect against the particular hazards of aircraft fires. Curiously, impact

injuries are not the airman's major concern in a flight deck crack-up; he confronts his most pressing danger while freeing himself from the aircraft and escaping a ring of flaming fuel whose temperature can be as high as 1700° F. Analysis of recent aircraft accident records continue to reaffirm this fact, and indicate that the greatest number of fatalities occur in accidents involving post-crash fire. Of the six basic factors which appear to be the basis for a reasonable crash survival theory, the post-crash fire hazard potential predominates and it alone has been rated as high as 35% for rotary wing aircraft.[1]

It therefore became obvious that fundamental to the aircrewmen's safety was the requirement for more effective fire-resistant clothing that could protect him during his dash through a blaze to safety.

Materials Development

Nylon has long served as the basic fiber in flight garments and life support equipment worn by aviators. Its advantages of high strength to weight ratio, durability, resistance to renovation procedures and versatility for adaption to various fabric constructions all were governing factors in its selection. However, conventional nylon poses a problem where intense heat is involved because it will melt at temperatures beginning at 480°F. This characteristic becomes a liability to the pilot in contact with flames, as the hot melting nylon sticks to the skin and increases the severity of skin burns.

Fire-retardant-treated cotton fabrics, although eliminating the hot/melt drip hazard of nylon in flight coveralls, present other problems, which also make it unsatisfactory for its intended use. The comfortable feel and absorbent qualities of the untreated cotton material is lost by addition of these chemicals which increase weight, stiffen the fabric, reduce air permeability, and often irritate the skin. Pilots when first issued a set of these treated coveralls were often found to wash them several times to soften the fabric. Unfortunately these, and subsequent washings, tended to reduce the fire-resistant properties of the treated material, and in addition, weakened the fabric so that it offered very little resistance to wear, tear and shredding. The poor serviceability of the Navy's earlier orange and khaki fire-retardant treated flight coveralls attests to the deficiencies of these treatments.

Obviously, the idea of an inherently fire-resistant fiber having the durability and strength of nylon without its hot melt/drip hazards was considered most desirable. An extensive evaluation program of "Nomex" was therefore begun by AMRD (Aerospace Medical Research Department) to determine the fiber's physical and thermal characteristics. This was then followed by a continuing research and development effort by engineers of the Naval Air Engineering Center to design flight clothing of "Nomex" materials specifically geared to provide maximum fire protection consistent with pilot comfort and service suitability.

"Nomex" proved to be far superior to any previously used materials for protective flight clothing. The main advantages are its inherent, permanent, flame resistance properties. The material does not support combustion and resists heat up to approximately 800° F. At this temperature it chars instead of melting, thus eliminating the hot melt/drip hazard associated with nylon garments. In addition, its abrasion, durability and washing qualities are excellent, comparing favorably with those of nylon. What this means to the Naval Aviator wearing a "Nomex" flight coverall, for instance, is that he never has to worry about his fire protection "washing out", as was the case in the previous standard treated cotton coveralls. The high temperature resistance property of "Nomex" is permanent and will remain throughout the life of the garment, which is estimated to be at least three times greater than the earlier cotton coveralls.

Current Status of Fire-Resistant Flight Clothing

1. *Coveralls, Flying, Summer, Fire-Resistant, Type CS/FRP-1.* Single standard issue for all pilots (FSN 8415-782-3199 Series). Replaces khaki and Indian Orange cotton coveralls (FSN 8415-264-8614 Series) and (FSN 8415-543-7862 Series) respectively. Initial pilot issue is two with one extra in case of extreme hot weather. Section H allowance listing—200% of non-pilot crewmembers of assigned aircraft, except 350% of non-pilot crewmembers of assigned helicopter squadrons deployed to combat zones.

Air Crew Systems Bulletin No. 127 dtd 8 Dec 1967 provides information and instructions relative to purpose, use, maintenance and repair of the "Nomex" coverall. (Note: Two-piece "Nomex" flight suits have also been authorized as the new standard for U.S. Army helicopter personnel (Southeast Asia) replacing U.S. Air Force (K-2B) cotton coveralls. The U.S. Air Force intends to adopt a

[1] Haley, J. L. Jr., Robertson, S. H., Turnbow, J. W. "Crash Survival Evaluation of the OH-4A Helicopter," 8 June 1965. AV SER M65-9 Aviation Safety Engineering and Research, Phoenix, Arizona, July 1965.

"Nomex" flight coverall design to replace their K-2B type cotton coverall and it has good standardization potential with the Navy coverall design.)

2. *Gloves, Flying, Summer, Fire-Resistant, Type GS/FRP-1.* Single standard issue for all pilots (FSN 8415-935-6328 Series). Replaces the all leather Navy B-3A glove and the interim U.S. Air Force cotton/leather Type (HAU-7/P glove. Section H allowance listing—120% of non-pilot crewmembers of assigned aircraft, except 150% assigned helicopter squadrons deployed to combat zones.

Air Crew Systems Bulletin No. 152 provides information and instructions relative to its purpose, use, and maintenance. (Note: The "Nomex"/leather Navy glove has been adopted by both the U.S. Air Force and U.S. Army and is now the standard single item of supply for all three services.)

3. *Suits, Flying, Winter (Jacket and Trousers) MIL-S-18342.* Current item, consisting of nylon outer shell, knitted polyester insulation and fire retardant treated cotton lining, will be replaced with all "Nomex" material components. Advanced development of an improved winter flight suit design using "Nomex" filament outer shall, "Nomex" quilted batting insulation and "Nomex" wrist and ankle knitted components has been completed. Fleet evaluation of prototype quantities is planned during winter 1969-70. Larger scale procurement of the finalized design will follow for introduction during winter 1970-71. The new item will then supercede present winter suit on an attrition basis.

4. *Coveralls, Anti-Blackout, Cutaway, Mark 2A Type, MIL-C-23955.* The present nylon cover fabric used to contain the bladders will be replaced with a "Nomex" fabric. A revision to the specification incorporating the new material components and necessary design changes are expected to be completed by June 1969 with future subsequent procurements reflecting the "Nomex" cover fabric substitution.

5. *Anti-Exposure Protective Clothing.* A new cold water exposure protective assembly has been developed using the skin divers "wet suit" principle of insulation. This assembly which incorporates the Navy's latest "Nomex" flying coverall as an overgarment will be distributed primarily to AIRLANT and AIRPAC HS and VS squadrons. A limited number of assemblies (500 of a 2,500 total) are also planned for closely monitored Fleet evaluation in VA and VF type squadrons. This assembly, by virtue of the integration of the "Nomex" coverall, has substantially improved fire protection properties over the present "dry type" MK5A anti-exposure garment. Evaluation of the "wet suit" assembly during FY 69 and 70 will determine its potential, as a successor to the MK5A suit. (See article on New Wet Suit below.)

Another cold water protective anti-exposure assembly currently in the advanced development stage will also take advantage of the fire safety features of a "Nomex" material as an integral part of the garment. This development program was approved by CNO as a result of a Fleet engendered need for an "intermediate" (cold water) type anti-exposure suit which could also serve as a cold weather flying suit. Prototype garments have been constructed in-house at ACED (Aerospace Crew Equipment Department) and will be flight tested during FY 69. Larger scale procurement for Fleet evaluation is expected to follow in FY 70.

Future Plans

As a result of recent tragic aircraft carrier fires the need for fire protection has been extended to include all shipboard flight and hanger deck personnel. NAVAIR will determine the specific requirements for protective clothing and equipments in this area and submit them to the various cognizant System Commands which have the technical development responsibilities. It is expected that "Nomex" materials will find a useful place in the design of some of these new special purpose clothing items that may be required.

"Nomex" knitted underwear constructions in combination with "Nomex" flight coveralls have been found, through laboratory tests, to provide the required thermal radiation protective qualities needed to prevent skin burns in the event an aircrewman is exposed to high thermal radiation. This underwear has been selected as part of the special equipment requirements for use by aircrewmen of nuclear strike aircarft. As recommended by APSET and approved by CNO further evaluation of "Nomex" underwear to determine its potential use as a replacement for the present standard issue cotton long underwear types will also be conducted.

Current and proposed "Nomex" fabric constructions have been under a continuing refinement and product improvement program to remedy some of their original shortcomings e.g. harsh feel, limited colors because of poor dyeing affinity, and a propensity for static electricity build-up.

Investigation of both new and improved fire-resistant fibers will continue at the Naval Air Development Center laboratories. One experimental new

high temperature-resistant fiber called PBI (polybenzimidazole) which shows promise, has been under development by the U.S. Air Force Materials Laboratory. Tests have shown it will not burn in air, has exceptional strength retention at high temperatures, and good heat transfer resistance. In addition, Air Force tests indicate PBI has almost three times the percent moisture regain of "Nomex" fibers, which could be a valuable factor in improving overall garment comfort. PBI, however, is *not* commercially available at this time, and is prohibitive in price to be considered for large scale use. Its progress will be closely watched in the hope production capability by industry will be obtainable.

(Editor's Note: At the present time the Air Force Life Support SPO has some 20 flight suits of various weights and weaves, manufactured from PBI, which they will test and evaluate over the next year. They plan to have prototype suits available for operational test and evaluation by next February.)

Summary

The successful incorporation of "Nomex" fabrics into environmental protective flight clothing has greatly enhanced the fire protection safety of Naval aircrewmen. This has been accomplished under a planned development program with the cooperation of industry and close coordination with the other services. "Nomex" summer-weight flight coveralls and gloves have been established as standard Navy supply items. Standardization of the gloves with the U.S. Air Force and U.S. Army has been accomplished and a standard Navy/Air Force summer-weight flight coverall is a possibility in the near future. Introduction of "Nomex" anti-blackout garments, winter flight clothing and new anti-exposure protective assemblies are planned within two years on a systematic basis.

Although "Nomex" clothing will resist flames and act as a good insulator in an emergency-fire-quick-escape situation, it should not be compared to garments designed for fighting fires. Obviously, heavier or double layer fabric constructions would proportionately increase fire protection but it then becomes a question of trade-off with a pilot's physiological tolerance.

The Navy's "Nomex" flight clothing provides the best overall fire protection to the aircrewman for the present and near term future in terms of: economics, compromise with comfort, reliability and useful service life. When used properly, it has increasingly proven itself as an effective means of allowing aviators to escape from post-crash aircraft fires with minimized skin burns and in some cases with their lives.

NEW WET SUIT TO BE FLEET-TESTED

A limited quantity of anti-exposure suits which are expected to increase the possibilities for survival of Navy aircrewmen downed in cold waters have been purchased for evaluation.

Based on the skindiver's "wet suit" principle, the air-ventilated wet suit (VWS) introduces a new concept in constant wear, cold-water anti-exposure protection for aircrewmen. The VWS has been designed specifically for pilot-cockpit compatibility and uses an integrated air-ventilation system as part of the suit. During the past winter a small quantity of these suits were supplied to AIRLANT squadrons for evaluation purposes. By June 1969 a total quantity of 2,500 suits will have been delivered to Atlantic and Pacific fleet squadrons (mainly VS/HS), for user-acceptance evaluation and as a possible successor to the MK-5A dry-type anti-exposure suit now operational in the fleet.

The VWS is a one-piece coverall designed with a front reversible entrance zipper plus zippers for the arms and legs. It is designed for continuous wear in aircraft where compatible air-ventilation systems are available. It is intended to provide the wearer protection from cold water, wind and spray. The chief advantages of the VWS over the MK-5A include less bulk, greater comfort, increased durability, and a higher degree of reliability during aircraft exit and immersion. (For further details on the VWS, see article "Divers' Wet Suits for Aircrew Personnel" in *Naval Air Systems News,* Vol. 1, No. 4, pp. 25-29.)

"NOMEX" GLOVE

Description: The glove is constructed with a soft cabretta gray leather for the palm and frontal portion with a stretchable type green polyamide fabric for the entire back portion. This glove replaces the all leather B3A glove. The leather used in the subject glove is a non-slip type, especially when wet. The fabric portion of the glove is a high temperature resistant and inherently flame retardant synthetic fabric with no hot melt or dip characteristics. This fabric will not support combustion but will begin to char at 700° to 800° F.

Size and Fit: Since the fabric portion of the glove is stretchable, five sizes (7 to 11 inclusive) are con-

sidered sufficient to accommodate the entire population. The subject glove has been designed to permit a snug fit and to provide sufficient dexterity and feel so as not to interfere in any way with the operation of the aircraft, manipulation of switches, knobs and/or safety or parachute harness buckles, etc.

Laundering: The leather portion of the glove is a launderable type and the fabric portion is a drip-dry type. The gloves may be laundered with warm water and mild soap by any of the following methods:

1. Don the gloves and wash with soap and water in a similar manner as washing your hands. When gloves appear clean, rinse and remove from hands. Squeeze, but do not wring or twist gloves, to remove excess water. After removing excess water, place indivdual glove flat on a towel. Roll towel to cover glove, making sure that gloves do not come in contact with each other.

2. Use normal procedure for colored goods. The gloves may also be laundered at home or in a commercial type washer and dryer. Laundering in water up to 140° F maximum and tumble drying up to 180° F will not damage or shrink the glove.

NOTE: Do not use any type bleaching compound in laundering. To avoid excess wear on the gloves during washing and drying, make sure there are sufficient articles in the wash to absorb tumbling shock.

Repair: Repair of the subject glove should be limited to restitching open seams.

FLIGHT DECK VEST OPERATIONAL TEST

Recently a blueshirt was blown from a carrier flight deck during day flight operations. He was wearing one of the new flight deck flotation vests which had arrived only a few weeks earlier. The man inflated the vest just prior to hitting the water. The inflated vest provided excellent torso cushioning protection and the man's head and upper chest were held well out of the water.

All flight deck personnel should be informed that the flight deck flotation vest has been tested successfully in an operational environment.—COMNAVAIRLANT Weekly Safety Bulletin.

SAFETY SIGNS

The sign said "Wear your Goggles." How many times have you seen that and heeded it not?

Man has learned that he can use the silent command to convey a thought. That is why signs are so popular to the American public. Whether it be "Wet Paint" or "Keep Off the Grass," signs are used to remind all of us to do something.

In man's makeup, eyes play an important part in our everyday lives. In fact, they are so valuable that our government has arranged whereby those of us who need eye protection can have it. Regardless of the type of work performed, or kind of hazard that exists, there is always eye protection available.

Sometimes it is hard to educate man to protect his own. On the other hand, he will lay down his life for something he cherishes. Patrick Henry, that fiery patriot of Colonial days, is quoted as saying "Give me liberty or give me death." He was making a decision regardless of the outcome.

Like the sign said, "Wear Your Goggles," the reader (of the sign) has to make a decision. The wrong decision can be disastrous. The sign was erected so the reader could protect his eyes. Either protect them and enjoy the scenery or forget about goggles and lead a dog's life—a *Seeing Eye Dog*—that is.

What a price to pay, depending on the eyes of a dog to lead one around. Living in total darkness, darkness that could have been prevented if only a sign had been heeded.

To restore the sight to someone who has lost theirs, someone has to give an eye made by God, not one made by Man. Very few people are willing to part with their eyes, even after death.

It is considered the proper thing to do to make out a will. So as to distribute what one owns to those who will receive, as the maker of the will wishes it to be. So if you are not a firm believer in signs, make an arrangement with someone, your wife for instance, that she will carry out your wishes (just in case you are in an area that requires eye protection and you heed not), that she will do the following for you:

1. Lead YOU wherever you want to go.
2. Help YOU dress and eat.
3. Describe the scenery to YOU on your vacation.
4. Read to YOU instead of watching television.
5. Describe the way the children's eyes light up at Christmas and what their graduations and weddings are like.
6. Do all the work around the yard and garage that YOU used to do.
7. Teach YOUR little boy how to play ball, build model airplanes and fish and hunt.

8. Take YOU to all sporting events although she does not enjoy them.
9. Describe the latest fashions of which YOU were so fond.
10. SHE will not complain because the family income is now on a reduced scale.

While the world is your oyster, stand erect, square back those shoulders and render respect the Flag is due. Your Flag and mine because there was no mistake in the colors. Your eyes had told you it was Old Glory. Because when you read the sign "Wear Your Goggles" you protected your eyes, YOU were a firm believer in SAFETY SIGNS.—*Hot Dope* Sheet, 2nd MAW, MCAS, Cherry Point, N. C.

STOKE'S STRETCHER

The Stoke's stretcher, standard shipboard equipment, was invented by Charles F. Stokes (then LCDR, MC), more than 60 years ago. The original design has been so satisfactory that little change has been made. The stretcher consists of a rigid, wire-basket frame, shaped to fit the body; it is particularly well adapted for use in transporting patients up and down ladders as well as from and into small boats. Dr. Stokes was Surgeon General of the Navy from 1910 to 1914.

AVIATION EXAMINING ROOM PERSONNEL —HELP AND COOPERATION NEEDED

It is realized that the workload has increased all along the line from the field level to the Bureau level, and that personnel changes occur frequently requiring the training of new individuals. In a number of cases, the final product, the flight physical examination, leaves much to be desired.

A flight physical examination must be complete in order to serve its purpose. For example: The SF 88 submitted on a candidate for any of the flight programs cannot be approved if any information required by the Manual of the Medical Department, Article 15-67, 15-68, or 15-69, as appropriate, is omitted, illegible or incomplete. It must be returned with a request for additional information, i.e., correction, verification, or amplification. This is not a simple process, since in most cases, the applicant must be contacted and re-examined, resulting in a delay of approval for the applicant, or the loss of the applicant to another program.

Since all of us play on the same team, it should be of interest to all hands to eliminate as much additional work as possible. Your cooperation will be greatly appreciated.—AeroMed, BuMed.

NAMI PARTS WITH FLYING LAB

The Naval Aerospace Medical Institute, Pensacola, Florida, has had one of the few Douglas EA-1E Skyraider aircraft, which was used as a flying research laboratory by NAMI's Research Department. The plane was recently transferred to the Air Force.

There are about a dozen EA-1E's left in the Navy and they are being transferred to the Air Force. The aircraft can hold almost a ton of medical electronic equipment and scientists have used it for everything from brainwave tests to electrocardiograms in the air. Most recently the aircraft was used to obtain in-flight noise attenuation measurements of flight helmet and in-flight recordings of radio communications transmitted from the Institute's Acoustics Laboratory. Mr. John R. Forstall, Technical Advisor on this program, used a manikin head and an SPH-3B flight helmet to obtain the in-flight recordings and noise attenuation measurements.

Captain Richard H. Tabor, MC USN, a naval aviator as well as a naval flight surgeon, was the last pilot for the EA-1E. Doctor Tabor acted as research pilot during the past year while undergoing residency training in areospace medicine at the Institute. Doctor Tabor left the Institute at about the same time as did the Skyraider. Doctor Tabor was transferred to the Third Marine Air Wing, El Toro, California. — *Capsule,* NAVAEROSPMEDCEN, Pensacola, Fla., Vol. 5, No. 5, Mar 7, 1969.

SAR EQUIPMENTS DEVISED BY NAS, JACKSONVILLE, FLORIDA

Medical personnel at the Naval Air Station, Jacksonville, Florida have devised, through modification of existing equipment, two items for use in SAR operations. The first of these involved modification to the semi-rigid, poleless Niel-Robertson litter that is employed in the NAS, Jacksonville SAR helicopter. These modifications included: (a) a shortening of the straps at the litter's apex that permits the loaded stretcher an additional six inches of hoist, thus making it easier to bring aboard the helicopter; (b) enlargement of the stretcher hood so that it can accept the injured with helmet on. This provides more safety to the injured since the clearance between the hoisted individual and the helicopter is very little. It also permits loading of the injured without removing his helmet which would be a danger if neck trauma were involved; (c) a "grasp loop" has been incorporated in the back of the

stretcher that would be even with the scapula. This facilitates drawing the loaded stretcher into the helicopter with one hand while the person operates the hoist with the other. The litter has been used in drills and has proven quite satisfactory. The second item was a modification of the SV-2 vest to provide an emergency medical pack which can be worn by flight surgeons on SAR missions. When loaded the vest weighs about 10 pounds. The following inventory of the four compartments of the vest is provided for suggestions to other flight surgeons:

Flight Surgeon Kit/Vest

Front Comp.:

- 2 Tube, glass, screw cap, Lithium Oxalate
- 2 Tube, glass, vacuum, red rubber stopper, Clot Tube
- 1 Tube, glass, vacuum, lavender rubber stopper, Oxalate Tube

Left Front Comp.:

- 1 Cuff, Blood Pressure
- 1 Flashlight with batteries
- 1 Laryngoscope
- 1 Stethoscope
- 1 Safar Airway
- 2 Oropharyngeal Airway (large/small adult)
- 1 Scissors, Bandage

Left Side Comp.:

- 4 Dressing, Medium
- 1 Dressing, 4 x 7
- 1 Dressing, Head
- 2 Dressing, 4 x 4 Compress
- 2 Bandages, Triangular
- 4 Eye Patches
- 1 Tape, 3″
- 2 Endotracheal tube, 34 & 38 Fr.
- 2 Tracheotomy Cannulas, #4, #6

Right Front Comp.:

- 1 Radio, RT-60
- 1 Pencil, marker
- 2 Needles, 13 ga., specimen

Right Side Comp.:

- 1 Splint, pneumonic, arm
- 2 Splint, wire
- 1 Tracheotomy set, field
  - 1 Handle, scalpel, #3
  - 1 Forceps, rat-toothed
  - 1 Hemostat
  - 1 Needle Holder
  - 1 Scissors, straight Mayo
  - 1 Hook, trachea
  - 3 Blades, #10
  - 2 Blades, #11
  - 1 Blade, #12
  - 2 Blades, #15
  - 2 Suture, atraumatic, Chromic, 4-0
  - 2 Suture, atraumatic, Silk, 4-0
- 4 Tourniquet, Rubber Tube
- 2 Syringe, 30 cc
- 2 Syringe, 2 cc, with needle
- 4 Needle, 20 ga.
- 10 Bandaid
- 10 Ammonia capsules
- 5 Morphine Syrettes, 15 mg
- 1 Xylocaine, 50 cc
- 1 Epinephrine, 30 cc
- 1 Tetracaine Ophth. Soln. 10 cc

(Editor's Note: Flight Surgeons interested in one or both of these modified units should contact the Medical Department, Naval Air Station, Jacksonville, Florida for additional information and/or photographs.)—Medical Committee, Aviation Safety Council, Southern.

EDITOR'S SECTION

MEETING OF THE SOCIETY OF MILITARY ORTHOPEDIC SURGEONS

The Society of Military Orthopedic Surgeons (S.O.M.O.S.) will hold its eleventh meeting at the National Naval Medical Center, Bethesda, Maryland 20014, on 22 through 24 September 1969.

Professional papers are requested for presentation at this meeting and further inquiries may be ad-

dressed to Captain Robert H. Brown, MC USN, Naval Hospital, Bethesda, Maryland 20014.

Reserve Officers are invited and may apply for this meeting via their district command.

SHORT COURSE IN ORTHOPEDIC PATHOLOGY

The annual six weeks short course in Orthopedic Pathology at A.F.I.P., Washington, D.C. will be given from 29 September through 8 November 1969. Eligibility for attendance is restricted to regular medical officers of the Army, Air Force and Navy presently assigned to full-time residency training in Orthopedic Surgery, preferably at third or fourth year level. Eligible Naval Medical Officers are reminded that the annual S.O.M.O.S. meeting will be held at National Naval Medical Center, Bethesda, Maryland 22-25 September; therefore, individuals or commands should make application for T.A.D. orders for inclusive dates of both the meeting and the short course (22 September through 8 November 1969). Applications should be forwarded immediately to BUMED Training Branch, Code 316, Navy Department, Washington, D.C. 20390.

SECTION OF MILITARY MEDICINE OF THE AMERICAN MEDICAL ASSOCIATION

The Section on Military Medicine of the American Medical Association has announced its tentative program for the annual convention to be held in New York City, 13–17 July 1969. On the program, which covers a variety of subject matter and denotes the versatility of military medicine, are several presentations by Navy Medical Department officers. Commanding officers are requested to encourage members of their staff who are going to the AMA meeting to attend the sessions of the Section on Military Medicine.

KNOW YOUR MEDICATIONS — "ZACTIRIN"

Plain "Zactirin" is a misleadng commonly used misnomer. If the item's composition is not clearly known, prescribing "Zactirin" for one with salicylate sensitivity may cause great distress. "Zactirin" is a *combination of ethoheptazine citrate and aspirin.*

The misnomer has resulted from a comparison of the "Zactirin" tablet and the "Zactirin Compound-100" tablet.

To establish proper identities, here are the popular Wyeth products:

"Zactane", 75 mg ethopheptazine citrate per tablet.

"Zactirin", 75 mg ethoheptazine citrate *and* 325 mg aspirin per tablet.

"Zactirin Compound-100", 100 mg ethoheptazine citrate, 227 mg aspirin, 162 mg phenacetin and 32.4 mg caffeine per tablet.

"Zactane" is the item to be prescribed if the desire is for analgesia of *only* ethoheptazine citrate.

Prescribe "Zactirin" by its generic name "Ethoheptazine and Aspirin" and there can be no error in its composition.

AWARDS AND HONORS

Navy Cross

Casey, Robert M., HM3 USN
Cruse, James D., HN USN
Gerrish, Alan R., HN USN
Powell, Richard L., HN USN

Distinguished Service Medal

Brown, Robert B., VADM MC USN
Burkley, George G., VADM MC USN (Ret)

Silver Star Medal

Burnley, Earl R., Jr., HM3 USN
Machmer, James A., HM3 USN
Sell, Robert R., HM1 USN
Sullivan, Caleb J., HM2 USN
Teague, Michael A., HM3 USNR
Watson, Donald P., HM3 USN
Wean, Douglas L., HM3 USN
Youngblood, Roy L., HM2 USN

Legion of Merit

Herrmann, Robert S., CAPT MSC USN
Kaylor, Jack N., HN USN
Markowitz, Herbert A., CAPT MC USN
Robinson, Donald W., CAPT MC USN

Navy and Marine Corps Medal

Coombs, Charles V., Jr., HN1 USN
Ray, Thomas P., HM3 USN

Bronze Star Medal

Burton, Jonny D., HN USN
Carroll, William E., HN USN
Casey, Thomas E., HM3 USNR
Chabot, Robert J., HM3 USN
Champine, Michael H., HM3 USN

Constantine, Miles E., HM3 USN
DeShazo, Claude V., LT MC USNR
Fox, Arthur L., HN USN
Fox, George C., HM2 USN
Frazier, Billy J., HN USN
Hines, Kenneth F., LCDR MSC USN
Lang, Maynard A., HMC USN
Long, Gregory R., HM2 USN (2nd Award)
Magness, Michael W., HM2 USN
Miller, Norman E., HN USNR
Moore, Maxie L., Jr., HM3 USN
Petersen, Edwin B., HM2 USN
Robinson, Rodney L., HM3 USN
Schnell, Stuart D., HM2 USNR
Seymour, Dalton G., HM3 USN
Stougard, John N., HN USN
Strasser, Wilbur J., HN USNR

Navy Commendation Medal

Baird, Robert W., HM3 USN
Bell, Willis H., II, LT MC USNR
Berghage, Thomas E., LT MSC USNR
Brasten, Anthony L., HM3 USN
Busch, Roger W., HM USN
Cannon, Mary, CAPT, NC USNR
Chitwood, Edward M., HMCM USN
Clark, James L., LCDR MSC USN
Clem, Doyne C., HM1 USN
Farmer, Gerald W., HM1 USN
Glazier, Wallace E., HM2 USN
Gutekunst, Richard R., CDR MSC USN
Hankey, Lorraine, CDR NC USN
Howard, John E., CDR MSC USN
Keller, Darrel J., HN USN
Kinder, James D., HM1 USN
Lawson, Donald R., LCDR MSC USN
LoDolce, Richard F., HM3 USNR
Miller, Lloyd W., CAPT MSC USN
Oldham, Richard T., HMC USN
Parker, Andrew J., HMC USN
Partridge, James S., HM2 USN
Pease, Isaac M., III, HN USN
Raasch, Frank O., Jr., CDR MC USN
Rayno, Robert H., LTJG MSC USN
Schwab, James A., HM1 USN
Siggers, Adolph L., LTJG MSC USN
Smith, Marcella, CAPT NC USN
Snittjer, William J., LT MSC USN
Sullivan, Raymond R., CAPT MSC USN
Turville, William C., CAPT MC USN
Yount, Jimmy R., HM2 USN

Navy Achievement Medal

Appleby, William C., HM2 USN
Barbarick, Donna L., LT NC USN
Bruce, Alyous S., HMC USN
Butler, Anna T., CDR NC USN
Colvin, William P., HMCM USN
Dickens, Jack C., HMCS USN
Jones, John H., HN USN
McKiernan, James J., HN USN
O'Brien, Robert L., HMCS USN
Olliff, Benjamin C., Jr., LT MC USN
Perry, Joe E., Jr., HM2 USN
Rees, John W., Jr., HM2 USN
Schroeder, William H., LCDR MSC USN
Segall, Harvey, HM1 USN
Weber, Lawrence H., Jr., HMCM USN

Letter of Commendation

Backer, M. H., Jr., CDR MC USNR-R
Beam, Walter E., CDR MSC USN
Butler, Anna T., CDR NC USN
Gobbel, Henry D., LCDR MSC USN
McDowell, Bruce R., HM3 USN
Long, James J., HM1 USN
Perry, H. O., CDR MC USNR-R
Rulon, David B., CAPT MC USN

Letter of Appreciation

Copeland, Winifred L., CDR NC USNR
Wilson, Elizabeth A., LCDR NC USNR

Vietnamese Armed Forces Honor Medal, 1st class

Kaufman, Louis R., CDR USN

DRAMATIC IMPROVEMENT OF PERIPHERAL VASCULAR DISEASE

Government scientists have reported dramatic improvement of peripheral vascular disease associated with Type III lipid transport disorder following administration of clofibrate (Atromid-S, Ayerst), but they have cautioned against scattergun therapy with this highly publicized lipid-lowering compound.

Investigators at the National Heart Institute, the National Institutes of Health, Bethesda, Maryland, reported results of their studies at the 41st Scientific Session of the American Heart Association, Bal Harbour, Florida, November 21-24 and in a recent issue of the *New England Journal of Medicine.*

Previously reported studies by the NHI team, headed by Drs. Donald S. Fredrickson and Robert I. Levy, have indicated that high cholesterol or triglyceride levels in the blood may be symptomatic of any of at least five different lipid-transport disorders, each differing not only in symptoms and prognosis, but also in basic mechanism and responsiveness to treatment. Although these disorders have often been previously lumped together under the general heading of "hyperlipemia", treating them as one disease is analagous to treating measles, mumps or chickenpox as a single infectious disease.

Drs. Robert F. Zelis, Dean T. Mason, Eugene Braunwald, and Levy reported that patients with Type III are particularly susceptible to development of peripheral vascular disease (PVD) and that objective improvement of PVD follows drug treatment of this lipid transport disorder. Although coronary artery disease is common in patients with Types II, III, and IV hyperlipoproteinemia, the occurrence of PVD had not previously been established. The NHI physicians studied five patients before and after 3-5 months of treatment with a therapeutic diet and clofibrate. Objective measurement of improvement following therapy in the most severely affected extremity indicated a dramatic increase in maximum bloodflow to this limb.

Few side effects to clofibrate treatment have previously been reported, but studies by Drs. Terry Langer and Levy suggest that muscle inflammation (myositis) and liver enlargement are potential hazards directly related to long-term administration of clofibrate. The NHI investigators reported in the *New England Journal of Medicine* that the acute muscular syndrome secondary to clofibrate use may have important ramifications.

While the mechanism of action of the drug is not clear, its principal effect is a reduction of the glyceride-rich, very low-density ("pre-beta") lipoproteins and, to a much lesser extent, of the cholesterol-rich, low-density ("beta") lipoproteins. This accounts for the clinical observation that the drug is extremely effective in patients with elevations in cholesterol and glycerides associated with Type III hyperlipoproteinemia and less effective in patients with Type II hyperlipoproteinemia.

Recent data suggest that cholestyramine rather than clofibrate is the drug of choice in Type II. Cholestyramine (Cuemid, Merk; Questran, Meade Johnson) forms complexes with bile acids in the lower intestine. These complexes are excreted in the feces. Bile acids are manufactured from cholesterol. The increased loss of bile acids resulting from cholestyramine causes increased amounts of cholesterol to be diverted into bile acid production to make good these losses. This results in lowering of blood cholesterol levels.

Further studies are needed to evaluate the efficacy of clofibrate in patients with Types IV and V.

The results of these studies suggest that clofibrate is effective against Type III hyperlipoproteinemia. In all cases, the effect of the drug seems to be enhanced by concomitant use of a proper therapeutic diet. Clofibrate therapy, however, is not without side effects; thus the type of hyperlipoproteinemia one is dealing with should govern its selection as a therapeutic agent.

Moreover, the NHI scientists strongly suggest that physicians closely monitor and examine all patients on long-term clofibrate therapy for abnormalities in muscle enzymes and evidence of muscle dysfunction and/or tenderness.—USDHEW, PHS, NIH, National Heart Institute, Bethesda, Md.

ARTHRITIS REHABILITATION SERVICES

Thousands of men and women now crippled with arthritis will receive improved rehabilitation services through a cooperative agreement between The Arthritis Foundation and the Social and Rehabilitation Service, Department of Health, Education and Welfare.

"About 13 million Americans report that they suffer from some form of arthritis. Over 10 million claim that they have seen a doctor about the disease. Over 3 million report that it limits their usual activity," said Miss Mary E. Switzer, Administrator of the Social and Rehabilitation Service.

"Government agencies have estimated that $393 million a year is paid under Federal laws to persons disabled by arthritis. Effective coordination between our two agencies will result in a program to hasten the rehabilitation of arthritis patients, and increase opportunities for their return to employment," Miss Switzer said.

The Rehabilitation Services Administration of SRS and The Arthritis Foundation each will appoint a representative to coordinate activities resulting from the agreement. The agreement has five objectives:

—To speed referral of persons who may benefit from assistance provided by either organization.

Both parties will train staff at the community level who are familiar with The Arthritis Foundation and State vocational rehabilitation agency programs.

—To encourage development and sponsorship of continuing programs in educational institutions. Educational opportunties and materials will be provided, such as regional, State, and local inservice training programs; fellowships in medicine, rehabilitation counseling, physical therapy, occupational therapy, social work and other health fields; and courses by universities and other educational institutions. In addition, The Arthritis Foundation and the Rehabilitation Services Administration will cooperate on development of training publications and films for professional health personnel.

—To increase research and demonstration projects. Both groups will sponsor the exchange of information on research of mutual interest and concern.

—To educate the public. Appropriate organizations will receive pamphlets, films and other materials to improve understanding and acceptance of the capabilities of persons handicapped as a result of arthritis. Additionally, RSA and The Arthritis Foundation will hold conferences and seminars to educate the public about rehabilitation needs of arthritis patients.

—To provide consultation services on programs and problems of mutual concern, by The Arthritis Foundation, through its headquarters office, and the RSA.

Joseph Hunt, Commissioner of the Rehabilitation Services Administration, SRS, pointed out that persons with medical, psychological, social, economic, and vocational problems resulting from arthritis can benefit from vocational rehabilitation services, if eligible.

He noted that benefit payments, in a Public Health Services survey, indicate the measure of assistance required by arthritis sufferers. "The SRS welfare staff has estimated $47 million in payments, per year, to persons with this ailment," Mr. Hunt said. "Social Security Administration has paid $85 million; and the Veterans Administration, $261 million."—USDHEW, SRS, Rehabilitation Services Administration, Washington, D.C. 20201.

A CATHETER-TIP ELECTROMAGNETIC VELOCITY PROBE

Accurate and continuous measurements of the speed of blood flowing through various blood vessels in man have been obtained easily, and without surgical exposure of these vessels, by a tiny electromagnetic device borne on the tip of a narrow plastic tube (catheter) inserted into the bloodstream.

The device is called a catheter-tip electromagnetic velocity probe. Successful tests of its performance in 23 unanesthetized patients were reported at the Scientific Sessions of the American Heart Association, Bal Harbour, Florida, by Drs. Ivor T. Gabe, Dean T. Mason, Christopher J. Mills, James Gault, John Ross, Jr., Eugene Braunwald, and John P. Shillingford, of the National Heart Institute's Cardiology Branch, Bethesda, Maryland, and the Cardiovascular Research Unit, Hammersmith Hospital, London, England.

The extensive clinical trials at the National Heart Institute were preceded by three years of developmental work at Hammersmith Hospital. There Drs. Mills, Gabe, and Shillingford conducted tests of several prototype velocity probes in animals and, subsequently, in the venous system of man, using themselves as experimental subjects.

The catheter-tip probe resembles the most widely used type of electromagnetic device for measuring bloodflow—the cuff electromagnetic flowmeter— in that it capitalizes on the fact that a conductor (in this case, blood) moving through an electromagnetic field (the force field surrounding an electrically-energized wire coil) generates a potential difference between two electrodes mounted on each side of the coil. This difference is proportional to the amount of blood flowing through the electromagnetic field. However, in the cuff flowmeter the coil is incorporated into a plastic cuff which must be implanted around a blood vessel. Its electromagnetic field radiates inwardly to encompass the entire inner diameter of the vessel, so that it measures total bloodflow in the encircled segment.

The catheter-tip probe, on the other hand, is inserted into the vessel, not outside it; and blood flows around the probe, not through it. The magnetic field is produced by a coil wound parallel to the long axis of the probe, and the electric current is sensed by two platinum electrodes placed opposite each other on the coil. Thus, instead of recording total bloodflow, the catheter-tip probe measures instantaneous blood velocity and direction of flow in the immediate vicinity of the probe.

However, velocity can be used to calculate total flow when vessel diameter is known; thus the new device provides yet another dimension to the study of circulatory dynamics. And the scientists speculate that velocity measurements in vessels leading from

the heart may provide additional useful information about heart function.

The principal advantage of the method derives from the simplicity, ease, and safety with which measurements can be obtained from any part of the circulatory system accessible to cardiac catheters. Catheters can be introduced into all major blood vessels and most minor ones in the body without the need to expose the vessels surgically.

The tiny device, measuring only ½ inch long and 3/32 inch in diameter, is mounted in the end of a narrow 4-foot-long catheter. It is capable of recording both the velocity and pressure of the blood simultaneously.

In the 23 patients studied by the NHI scientists, bloodflow velocities were measured in the aorta, vena cavae, and pulmonary arteries. Velocity probes were passed to these sites by way of vessels in the arm. This enabled the scientists to measure, directly via an intravascular route, normal blood velocity and its acceleration or deceleration in response to various normal stimuli and maneuvers. These included respiration, leg exercise, and the Valsalva maneuver (attempted forced expiration with the mouth and nose closed). They were also able to determine hemodynamic responses to various disease states and to heart stimulants.

For example, in one patient suffering from cardiac tamponade (abnormal accumulation of fluid between the heart and its outer membranous sac that restricts heart motion), removal of this fluid increased aortic blood velocity from 48 to 83 centimeters per second. Drs. Gabe and co-workers report that no complications occurred through use of the velocity probe in these patients.

From these studies, the scientists conclude that their intravascular velocity probe constitutes a new and practical approach to the study of heart and circulatory functions in man, and it promises to become a valuable new addition to routine diagnostic catheterization procedures in conscious human patients for mapping the location and extent of derangements in these functions.

(The velocity probe is manufactured by S. E. Laboratories, Feltham, Middlesex, England.)—USDHEW, PHS, NIH, National Heart Institute, Bethesda, Md.

VENEREAL DISEASE

Attention of all Medical Department personnel is invited to the revision of SECNAV INSTRUCTION 6222.1B. The new instruction, SECNAV INSTRUCTION 6222.1C, subject: "Repression of prostitution and control of Venereal Disease" was signed by the Secretary of the Navy on 26 February 1969.

The major addition to this Instruction is the delineation of diseases which are to be classified as "venereal diseases," i.e., those which are listed in Categories 020-.... through 039-.... of the Department of Defense Disease and Injury Codes, NAVMED P-5082 Part 1. These categories include syphilis and gonorrhea and complications associated with these two diseases, chancroid, lymphogranuloma venereum and granuloma inguinale.

Provision for prophylactic *treatment* upon request of personnel with a history of exposure to possible venereal disease is retained in the current Instruction. Prophylactic treatment under these circumstances is aqueous penicillin 2.4 million units I.M. for males and 4.8 million units for females. An alternate drug should be used in persons with a history of penicillin sensitivity. This regimen is intended primarily for the prophylactic treatment of gonorrhea, however, ongoing clinical studies have suggested the effectiveness of such a regimen preventing syphilis as well. However, until the evidence for this is more concrete, patients treated prophylactically for gonorrhea should be followed-up for syphilis at appropriate intervals.

Among other aspects of venereal disease control discussed in this Instruction are the following:

1. Provisions necessary for the repression of prostitution.

2. Emphasis on continence as the only *sure* method of avoiding infection.

3. Requirement for lectures on sex-hygiene and venereal disease control.

4. Necessity for infected individuals to report promptly for medical evaluation.

5. Elimination of use of punitive measures in venereal disease control.

6. Information obtained during the case interview and contact investigation must be considered privileged information.

7. Prompt reporting to federal, state, or local health departments or other military facilities of all contacts is essential.—TB-Venereal Dis Con Sec, BuMed.

DEPARTMENT OF THE NAVY

BUREAU OF MEDICINE AND SURGERY
WASHINGTON, D.C. 20390

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